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proach drawn from the two trials would be to employ a loading dose of clopidogrel in STEMI patients up to age 75 who present within 24 hours of symptom onset, and to skip the loading dose in patients beyond that age, since there is good evidence of efficacy for the 75-mg dose in the very elderly from COMMIT but no safety data for a loading dose in that age group, said Dr. Cannon of Brigham and Women's Hospital, who together with Dr. Sabatine was co-principal investigator in CLARITY.

Dr. Cannon added that the worldwide public health implications of this new addition to the management of STEMI are profound.

Two weeks of clopidogrel costs \$50-\$100—compared with several thousand dollars for a single dose of a modern fibrinolytic agent—placing dual antiplatelet therapy within reach of many patients, even in developing countries.

"The evidence provided by these two studies with 50,000 randomized patients is very, very strong," Dr. Cannon told this newspaper. "Obviously I can't speak for the [American College of Cardiology/American Heart Association] guideline committee, but I have heard members of the committee say these studies provide about as strong evidence as you would want to add a new treatment to the guidelines for management of STEMI."

The combination of clopidogrel and aspirin has previously been shown to reduce coronary risk in patients with unstable angina and in those undergoing percutaneous intervention. An ongoing study that has completed enrollment is examining whether adding long-term clopidogrel is of benefit in a broad group of patients with high-risk vascular disease.

CLARITY was funded by Sanofi-Aventis and Bristol-Myers Squibb Co. Dr. Sabatine and Dr. Cannon have served on paid advisory boards for both companies. COMMIT was funded by those companies along with AstraZeneca, the British Heart Foundation, and the U.K. Medical Research Council. ■

Fish Oil Supplements Touted as Alternative to Treat High Triglycerides

BY BRUCE JANCIN
Denver Bureau

COLORADO SPRINGS — Omega-3 fatty acid capsules are an excellent alternative to the traditional fibrates or niacin for triglyceride lowering, John A. Merenich, M.D., said at a meeting of the Colorado chapter of the American College of Physicians.

"I am a huge advocate of the omega-3 fatty acids. If you haven't been using them, you've really got to try it," asserted Dr. Merenich, an endocrinologist who directs population-management programs for Colorado Kaiser Permanente in Denver.

The American Heart Association recommends consumption of at least 1 g/day of the omega-3 fatty acids docosahexaenoic acid (DHA) and/or eicosapentaenoic acid (EPA) to reduce cardiovascular risk in patients with established coronary disease, and at least 2 g/day to treat hypertriglyceridemia.

It's tough to get that much by eating fish. Besides, there is growing concern regarding the adverse health effects of eating large quantities of fish possibly contaminated by mercury, polychlorinated biphenyls (PCBs), and other toxins.

In nature, fish obtain omega-3 fatty acids by consuming large quantities of DHA/EPA-producing algae and plankton. When cost isn't an issue, Dr. Merenich's preferred source of omega-3 fatty acids is the DHA oil capsules produced by Martek Biosciences Corp. Martek has developed proprietary technology to grow large quantities of a

DHA-rich microalgae, bypassing the middleman—that is, the fish—altogether.

"You don't have to kill the fish, you don't have to worry about the organic solvents, the mercury, dioxins, whatever. The PETA [People for the Ethical Treatment of Animals] people are happy. Everybody's happy," he said.

It's a very well-tolerated product. The downside is it's quite expensive, at a cost of about \$2/day.

Fish oil capsules are much cheaper. But it's important to understand that a 1-g capsule of fish oil typically contains only 300

mg of DHA/EPA. So to obtain 2 g of the triglyceride-lowering active ingredients, a patient has to swallow 6 or 7 capsules per day. Still, Dr. Merenich has found most patients are much more willing to do that than to take conventional, side-effect-laden niacin for triglyceride lowering.

"Niacin is a pain in the rear end," he declared, noting that he is successful in keeping patients on long-term niacin therapy only

about 60% of the time. Fish oil supplements are distilled to achieve purity. Concerns about contamination by mercury, PCBs, or dioxin haven't been borne out in lab studies conducted by Consumer Reports and ConsumerLab.com.

Consumer Reports evaluated 16 brands of fish oil supplements in its July 2003 issue. None were contaminated. All contained the claimed quantities of omega-3 fatty acids. The review concluded it's reasonable to choose a product based upon low cost and listed two as "best buys": Kirkland Signature Natural Fish Oil, avail-

able at Costco, and Member's Mark Omega-3 Fish Oil, sold at Sam's Club.

More recently, ConsumerLab.com tested 41 commercially available fish oil products. Again, none were contaminated by the environmental toxins that are increasingly concentrated in many fish species.

"The GNC and Vitamin Cottage products are very, very good and priced reasonably. I refer patients there," said Dr. Merenich, who disclaimed financial interest in the products he discussed.

He added that the omega-3 fatty acids lend themselves particularly well to combination lipid-lowering therapy with statins. Many patients like the idea of taking a nonprescription 'natural' product along with their prescription drug. While statins primarily target LDL, in higher dosages they can also lower elevated triglycerides by 25%-35%.

Another reason to consider combination therapy is that a patient's LDL level often increases after initiating triglyceride-lowering therapy. "That's a common clinical situation. I probably get this question more than any other," he said.

Even if the LDL does go up, the cardiovascular risk as reflected in the non-HDL cholesterol level is often reduced by effective triglyceride lowering. And non-HDL cholesterol is an even better indicator of risk than LDL, particularly in patients with metabolic syndrome.

Consider, for example, a patient with metabolic syndrome who has a baseline total cholesterol of 186 mg/dL, a triglyceride level of 258 mg/dL, an LDL level of 98 mg/dL, and an HDL level of 36 mg/dL. After 3 months of triglyceride lowering, total cholesterol is 179, triglyceride is 142, LDL is 113, and HDL is 38 mg/dL. That patient's baseline non-HDL cholesterol was 150 mg/dL; after treatment, it has dropped to 141 mg/dL. ■

Fish oil supplements are distilled to achieve purity. Concerns about contamination have not been borne out in independent lab studies.

1 in 12 MIs Present With Life-Threatening Noncardiac Condition

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — One in 12 patients with acute MI presents with a concomitant acute potentially life-threatening noncardiac condition, Judith H. Lichtman, Ph.D., reported at the annual meeting of the American College of Cardiology.

None of the current risk-adjustment models for MI patients that are widely used to guide clinical care and benchmark hospital and physician performance take account of these life-threatening noncardiac conditions.

Instead, the prognostic models are restricted to variables directly related to the patient's cardiovascular disease. That's largely because the models were developed using data from random-

ized clinical trials from which patients with significant comorbidities are generally excluded. As a consequence, the risk-adjustment models fail to account for much of the variation in short-term outcomes in MI patients, explained Dr. Lichtman of Yale University, New Haven.

This is a glaring oversight, she stressed, because those one in 12 MI patients who have a dueling potentially life-threatening acute noncardiac condition account for a disproportionate share of total inpatient deaths. Indeed, in the Prospective Registry Evaluating Outcomes After Myocardial Infarction: Events and Recovery (PREMIER) study, they had an in-hospital mortality of 20%, compared with 3% in MI patients without such comorbidities.

"We feel that in this study

we've identified a very important subgroup of acute MI patients at increased risk for mortality that have really not been previously described in the literature," she added.

The PREMIER registry involved 3,948 acute MI patients prospectively enrolled at 19 participating U.S. medical centers during 2003-2004. Chart review showed 8% had an acute potentially life-threatening noncardiac condition at the time of admission. These were not chronic conditions such as arthritis or seizure disorders. The most common of these conditions included severe pneumonia requiring intubation, trauma, stroke, sepsis, severe GI bleeding, and hip fracture. Patients who present with one of these conditions in addition to an acute MI typically

require care from multiple specialists, both cardiovascular and noncardiovascular.

The MI patients with acute potentially life-threatening noncardiac conditions in PREMIER presented differently from those with MI alone. They were older—a mean age of 62 years compared with 56—and more likely to be women and nonwhite. They also were more likely to have diabetes and hypertension and less likely to present with ST-elevation MI.

After adjustment for the lesser use of guideline-based initial therapies for MI in the patients with potentially life-threatening comorbid conditions, along with differences in demographics, prior history, and clinical presentation, the study showed the patients still had a 4.9-fold increased

risk of in-hospital mortality.

"I think this underscores a strong need to adopt a broader perspective of the clinical factors that contribute to the initial assessment, process of care, and outcomes for acute MI patients. ... These factors need to be put on the radar of these risk-adjustment models," Dr. Lichtman concluded.

Session cochair Eric D. Peterson, M.D., of Duke University, Durham, N.C., who was a coinvestigator in the PREMIER registry, said that while most MI patients with an acute potentially life-threatening noncardiac condition are routinely admitted to coronary care units, it might make more sense for them to go directly to the intensive care unit, where caregivers are experienced in managing a wider array of very serious medical conditions. ■