Keep Aspirin Below 100 mg/day for Vascular Events

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — When it comes to prescribing daily aspirin for the prevention or treatment of vascular events, the lowest risk of bleeding complications in a new metaanalysis involving more than 192,000 patients was seen at dosages less than 100 mg/day, Victor L. Serebruany, M.D., reported at the annual meeting of the American College of Cardiology.

The most surprising finding in this massive meta-analysis was not that lower aspirin doses are safer—"You don't need to be a rocket scientist to realize that," he said—but rather, that the bleeding risk climbed dramatically with doses even in the moderate range of 100-200 mg/day. The analysis involved 31 randomized controlled trials published since 1988.

"We do not know if 75 mg/day of aspirin is better or worse than 325 mg in terms of efficacy, because there has been no direct comparative trial. However, now we know for sure that the lower the dose, the less the bleeding risk … The absolutely practical, simple lesson is, if you are not sure that efficacy is actually different, use as low a dose as possible," stressed Dr. Serebruany, owner of HeartDrug Research, LLC, of Towson, Md.

Of the 31 trials included in the meta-analysis, 9 featured low-dose aspirin arms. Eight examined the impact of moderate-dose aspirin, defined by Dr. Serebruany as 100-200 mg/day. Nineteen had high-dose aspirin arms, involving daily doses greater than 200 mg.

The rate of major bleeding was around 1.5% in patients on low- or moderate-dose aspirin, rising to more than 5% in the high-dose group. Surprisingly, however, the 0.47% stroke rate associated with moderate-dose aspirin was twice that of the low- or high-dose groups. The 2.7% GI bleeding rate in the moderate-dose group was nearly as great as that in patients on high-dose aspirin and significantly more than the 0.97% rate in patients taking less than 100 mg/day.

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DR. SEREBRUANY

Minor bleeding also was common among patients taking 100-200 mg of aspirin daily. As a consequence, the moderate-dose group had the highest rate of total bleeding complications, at 11.3%. This was somewhat greater than the total bleeding rate in patients on high-dose aspirin (just over 9%) and far more than the 3.3% rate in patients on low-dose therapy.

Why so many bleeding complications with moderate-dose aspirin? Dr. Serebruany suspects the answer lies, at least in part, in the use of more stringent adverse event reporting systems in some of the large, recent trials using doses of 100-200 mg/day. In the earlier studies involving high-dose aspirin, minor bleeding often went overlooked.

Dr. Serebruany estimated that at least three in five American men and two in five women over age 45 are taking aspirin. "One of every four patients after an acute vascular event will not develop another vascular event if taking aspirin. It would not be fair to say other antiplatelet agents are less beneficial or more beneficial. They are simply used on top of aspirin," he said.

The lower-is-better message when it comes to aspirin prescribing is particularly relevant for interventional cardiologists. They often aggressively pile on short-term use of multiple antiplatelet agents, antithrombins, and/or glycoprotein IIb/IIIa inhibitors in addition to moderate- or high-dose aspirin in an effort to minimize the risk of subacute thrombosis in conjunction with stenting.

Dr. Serebruany scoffed at this approach as platelet overkill and urged physicians who prescribe combination antiplatelet and/or anticoagulant therapy to keep the aspirin dose below 100 mg/day.

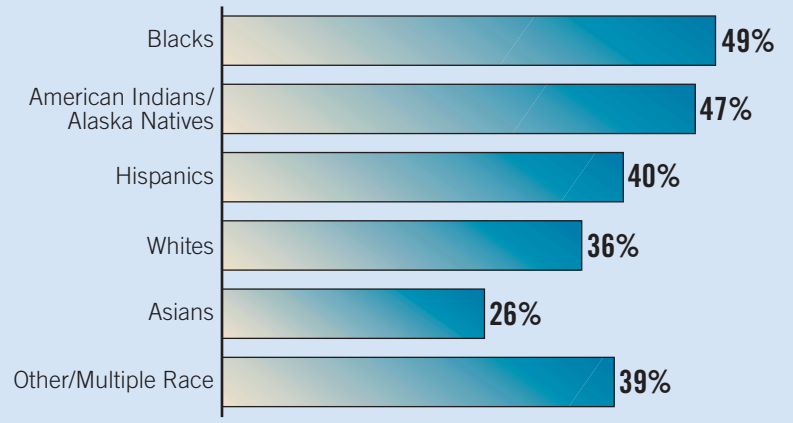
"If you give 25 mg of aspirin, you have complete platelet inhibition within 10 minutes. This is a fact. So why do you need more? It's probably overprotective," the physician said.

Besides, Dr. Serebruany added, there's not much evidence that this aggressive, higher-risk antiplatelet strategy on the part of interventional cardiologists is even achieving its purpose.

"The restenosis rate is definitely going down with the use of drug-eluting stents. However, the rate of subacute thrombosis isn't necessarily going down." ■

DATA WATCH

Racial/Ethnic Groups Reporting Multiple Risk Factors for Heart Disease, Stroke



Note: Based on a study of adults who reported having two or more of the following: high blood pressure, high cholesterol, diabetes, obesity, current smoking, or physical inactivity in 2003.
Source: Centers for Disease Control and Prevention

KEVIN FOLEY, RESEARCH/SARAH L. GALLANT, DESIGN

Try Using Omega-3 Capsules for Triglyceride Reduction

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. "I bat about 60% in keeping patients on niacin long term, and I spend a lot of time counseling them. Niaspan is much better tolerated, but it's quite expensive."

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. Consumer Reports listed two as "best buys": Kirkland Signature Natural Fish Oil, available 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 having any 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. Although 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," the physician said.

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