Extended-Release Niacin Blocks Postprandial HDL Reduction

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April 30, 2012 (Chicago, Illinois) — High-density-lipoprotein (HDL) cholesterol decreases significantly after an oral fat load. One-time dosing with either 1 or 2 g of extended-release (ER) niacin mitigated this decline in drug-naïve subjects.

These findings suggest that there are acute pharmacodynamic effects of niacin that are underexplored, said M. Haris Usman, MD, from the University of Pennsylvania in Philadelphia. He presented the results of 2 postprandial studies here at the Arteriosclerosis, Thrombosis and Vascular Biology 2012 Scientific Sessions.

Preliminary data suggest that these processes are subdued in the fasting phase. Because ER niacin is typically dosed at night, current dosing regimens might not be taking advantage of additional mechanisms of action.

He reported that the acute pharmacodynamic effects of ER niacin include lowering triglycerides, elevating angiopoietin-like protein 3 (ANGPTL3), and suppressing cholesterol ester transfer protein (CETP).

The session was moderated by Michael Davidson, MD, from the University of Chicago in Illinois. Although the presentation elicited a great deal of interest and questions from the audience, Dr. Davidson told *Medscape Medical News*, "I'm not sure what to make of it."

Dr. Usman began his talk by explaining that HDL cholesterol is inversely correlated with atherosclerosis. In contrast, postprandial dyslipidemia predicts atherosclerosis. Niacin is known as the most potent HDL elevator; therefore, the primary aim of the study was to evaluate whether ER niacin dosed before a fat challenge attenuates the postprandial drop in HDL cholesterol levels, compared with placebo.

He presented the results of 2 studies. The first was an open-label crossover pharmacodynamics trial comparing 1 g of ER niacin with a fat load without niacin. There were 304 fat challenges in 152 subjects.

The second was a double-blind placebo-controlled randomized crossover trial comparing 2 g of ER niacin with placebo. He described the subjects as very healthy, with a "very pristine hemodynamic and lipid profile."

In the first study, as expected, HDL levels dropped after the fat load alone, with an incremental area under curve (iAUC) of –71.9 mg/dLh (–65.1 to –78.6). One gram of niacin attenuated this reduction in HDL cholesterol to –32.5 mg/dLh (range, –25.6 to –39.3) — a 55% difference ($P < .00001$). He explained that "niacin not only attenuated this response, but caused an initial rise in apolipoprotein A1."

In the second study, the patients had an oral fat tolerance test. After a drug-free week, 2 g of ER niacin was even more effective at mitigating the drop in HDL cholesterol. The iAUC for placebo was –19.0 mg/dLh (–35.7 to –2.3) and for niacin was –2.1 mg/dLh (–18.8 to +14.6) — an 89% difference ($P = .047$).

In these patients, CETP activity was decreased with niacin, "suggesting that there clearly is a role for niacin in CETP inhibition in humans." Plasma ANGPTL3 was increased with niacin.

Dr. Usman explained that a dose-related effect on very-low-density lipoprotein levels was found with niacin. This effect was seen after 2 g. He concluded that "perhaps we are not exploring the effects of this drug the way we should be."

Other studies indicate that niacin is most effective >3g/day.

Dr. Usman and Dr. Davidson have disclosed no relevant financial relationships.

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