The Uncertain Role of Raising HDL-C with Niacin

At the end of May 2011, the National Heart Lung and Blood Institute of the National Institutes of Health (NIH) ended a large and widely-anticipated clinical trial that went by the acronym AIM-HIGH, but was formally called the Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health. The group of scientists responsible for monitoring the unblinded data felt that there was no point in completing this study since no differences between the niacin and placebo groups would be significant even if the study were carried to completion.

Does this mean that large doses of the vitamin niacin are of no value? Does this mean that raising good cholesterol (HDL-cholesterol) is not a good strategy?

AIM-HIGH was a trial of 3414 patients evaluating the addition of extended release niacin to optimal statin therapy (simvastatin) in patients with known coronary disease. Statins have been unequivocally shown to reduce major cardiovascular events in these patients. The question was whether niacin provided any incremental value in patients that additionally had lower HDL-C and higher triglycerides seen in patients with the so-called metabolic syndrome. Similar trials have suggested that statins plus niacin could indeed cardiovascular events, but no prior study compared that regimen to statins alone.

Note that the average triglyceride levels were not that significantly elevated (only 161 mg/dL) and the average HDL-C were not terribly low (about 35 mg/dL). It is unclear if most lipidologists would actually aggressively initiate niacin therapy in patients with these baseline lipid values already on optimal statin therapy with target mean LDL-C at 71 mg/dL. The HDL-C levels did increase by about 20% and triglycerides were lowered by about 25% in the niacin group. But these values do not represent the highest risk patients of interest to disease management specialists like myself.

The Data and Safety Monitoring Board responsible for stopping this study made this key decision, but the true data analyses and nuances of this trial will not be known for many months as these data are scrutinized and parsed to glean insights into the rhetorical questions I posited earlier. Was there a trend to benefit in those possibly higher risk patient subsets with higher triglycerides or lower HDL-C levels? Was the distribution of another lipid lowering agent (ezetimibe) to control LDL-C equitable and perhaps contributory? What about the small number of increased strokes in the niacin group (not statistically significant)? What about the subgroups with elevated lipoprotein(a), itself a risk factor that is affected by niacin? Undoubtedly, there will be new theories proposed and hypotheses to be tested in future trials, especially as we may be on the threshold of new agents that may promise even more remarkable lowering of bad cholesterol (LDL-cholesterol) and raising of good cholesterol (HDL-cholesterol). The proof will be in what are known as outcome trials that are targeted at sorting out whether the quality and quantity of life of treated patients are significantly improved. There is an ongoing trial called HPS2-THRIVE that should provide additional data in the future.

So it is premature to derive any conclusions about niacin therapy or its role in the raising of good cholesterol. There certainly no compelling data that raising HDL-C is not useful, although the methods used may be important. As we gather and analyze the details, clearer recommendations and strategies will undoubtedly emerge. Patients and doctors should not change treatment regimens based on these preliminary data.

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