Do patients on statins also need niacin?

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ABSTRACT

Niacin has been used for years to treat hypercholesterolemia, but may not be as beneficial as thought for patients at high risk of cardiovascular disease. Until further research is done, niacin should be used only in patients who do not tolerate or respond to statin therapy, and never in patients who have achieved goal LDL cholesterol on a statin.

Keywords: niacin, hypercholesterolemia, statin, LDL, HDL, cardiovascular

Vitamins have fascinated people for decades. The term "vitamin" was first coined by biochemist Kazimierz Funk in 1912 to mean "vital amine." All of these micronutrients were thought to be amines, but when that turned out not to be the case, the word was shortened to vitamin. For centuries, food nutrients have been connected with maintaining health and preventing diseases such as scurvy (vitamin C), night blindness (vitamin A), beriberi (vitamin B1), peripheral neuropathy (vitamin B6), and rickets (vitamin D). As a result, clinicians have been extending the benefit of vitamins to all areas of health. Just review the last decade of vitamin hype: vitamin D has essentially been glamorized to be the new fountain of youth. Take 2,000 units per day and you will live forever, never again to have a fracture, asthma, schizophrenia, or cancer. Vitamin E was once thought to be magic for older adults, a pure antioxidant that prevents oxygen free-radical destruction in the brain. We expected dementia prevention and less cancer, but instead got higher fall rates. For these vitamins, research has been disappointing and the clinical utility futile.

The newest vitamin to be challenged is niacin (vitamin B3, discovered in 1936), which has been used for years to treat hypercholesterolemia. This discovery came from the Coronary Drug Project study in 1975.[1] This study showed that niacin reduced recurrent myocardial infarctions (MIs) in patients with previous MI. The number needed to treat (NNT) is 30, meaning that for every 30 patients treated with niacin, one will not have a recurring MI. The niacin group had no change in cardiovascular mortality or all-cause mortality. Death rates were higher in patients on niacin who had cardiac rhythm disturbances such as atrial fibrillation.

Recently, the clinical focus on cholesterol treatment has shifted from continued LDL lowering to raising HDL levels in patients with controlled LDL cholesterol. Statins are excellent at lowering LDL cholesterol, but not raising HDL cholesterol. Niacin is just the opposite, excellent at increasing HDL cholesterol, but less effective in lowering LDL cholesterol. Practitioners have been using niacin in combination with statins to increase HDL cholesterol. Much of the excitement came from the HDL-Atherosclerosis Treatment Study (HATS) in 2001.[2] This small study of 160 patients over 3 years looked at change in stenosis on arteriogram (disease-oriented outcome) as the primary outcome and death and cardiovascular events as the primary clinical outcome. Group comparisons were simvastatin plus extended-release niacin, antioxidant vitamins, simvastatin plus extended-release niacin plus vitamins, or placebo. Primary clinical outcomes showed a reduction of clinical events in counts; 12 events in placebo group, 11 events in the antioxidant group, 6 events in the statin-niacin-antioxidant group and 1 event in the simvastatin-niacin group. This study has led many practitioners to recommend the addition of niacin to statin therapy.

A much larger patient-oriented outcome study called the AIM-HIGH trial was devised to confirm the results of the HATS and other trials.[3] This trial followed 3,414 patients taking simvastatin and ezetimibe if needed to keep LDL levels 40 to 80 mg/dL. Patients were randomly assigned to receive extended-release niacin or placebo. The trial was stopped early after a mean follow-up of 3 years due to a lack of efficacy on the composite endpoint; however, niacin increased median HDL from 35 to 42 mg/dL, lowered triglycerides from 164 to 122 mg/dL, and lowered LDL from 74 to 62 mg/dL. The primary composite endpoint assessed was death from coronary heart disease, nonfatal MI, ischemic stroke, hospitalization for acute coronary syndrome, or symptom-driven coronary or cerebral revascularization.

The results of the HPS2-THRIVE trial were presented at a recent American College of Cardiology meeting.[4] Many believe that this trial will end any clinical role niacin may have in high-risk patients with cardiovascular disease. This trial compared extended-release niacin plus the antiflushing

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agent laropiprant against simvastatin (alone or in combination with ezetimibe). Over 3.9 years, study participants were hospitalized with serious adverse reactions including excess bleeding, which had a number-needed-to-harm (NNH) of 142, meaning that for every 142 patients treated in the niacin group, one would have GI or intracranial bleeding. Other serious adverse reactions reported in the trial were serious infection (NNH 70) and new-onset diabetes (NNH 55). The study found no significant benefit on the primary outcome of major cardiovascular events when niacin was added to statin therapy. Because risk exceeds benefit, adding niacin to statin therapy cannot be recommended in patients with well-controlled LDL cholesterol. This trial is not yet published and data conclusions should be considered preliminary.

For now, restrict niacin use to patients who do not tolerate or respond to statin therapy, and never prescribe it to patients who have achieved goal LDL cholesterol on a statin. Next, seize the concept of "good-enough care." Get suitable patients on a statin, adjust the dose, be satisfied with the result, and help patients recognize other resources that may have a larger effect on their lives, such as saving money, making better food choices, and exercising. Lastly, recognize vitamins as poor prevention therapy for non-nutritional disease. Let's keep vitamins in perspective, and simply enjoy them in food for their nutritional value. **JAAPA**

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