Niacin added to statin therapy increases HDL cholesterol levels but does not improve HDL functionality, research shows

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While two large clinical trials recently showed that adding niacin to statin therapy failed to improve clinical outcomes despite a significant increase in HDL-C levels, little is known about exactly why the increased HDL-C levels did not reduce the risk of cardiovascular events, including heart attack and stroke. Now, a small study from researchers the Perelman School of Medicine at the University of Pennsylvania, has shown that while niacin increased measured levels of HDL-C, it did not improve the functionality of HDL. This may provide an explanation for the failure of niacin to further reduce cardiovascular risk. The study results were reported today at the 62nd Annual Scientific Session of the American College of Cardiology in San Francisco (Abstract # 919-7).

"There is a major need to identify additional agents to target residual cardiovascular risk beyond the use of statins," said senior study author Daniel J. Rader, MD, professor of Medicine and chief, Division of Translational Medicine and Human Genetics, at Penn. "Niacin is one of the oldest players in this field and is often used clinically to increase HDL cholesterol levels. However, much to the disappointment of the medical community, recent trials of niacin added to standard LDL-lowering therapy with statins failed to show benefit in improving cardiovascular outcomes. There has been substantial recent interest in the function of HDL independent of HDL cholesterol levels. We performed a small trial to examine how niacin modulated a classic function of HDL, namely its ability to promote cholesterol removal from

cells."

Previous work from Penn investigators has shown that a measure of HDL function, cholesterol efflux capacity, is more strongly related to coronary artery disease than HDL cholesterol levels.

To assess the change in functional capacity of HDL with niacin therapy, they randomized 39 patients with known carotid atherosclerosis to either simvastatin plus placebo or simvastatin plus extended-release niacin. After six months of therapy, they measured HDL-C levels and assessed functional properties using two tests – cholesterol efflux capacity (a measure of how well HDL removes cholesterol from lipid-loaded cells) and the HDL inflammatory index (which quantifies the antioxidant properties as it relates to preventing the oxidation of LDL).

As expected, they saw a 29 percent increase in HDL cholesterol with the addition of niacin to statin therapy, compared to a two percent increase in those treated with statin only. However, on the measures of cholesterol efflux capacity and the HDL inflammatory index, they saw no significant changes in HDL function.

"Based on our research, we now know that the addition of niacin to statin does not improve HDL function, providing a possible explanation for the failure of previous large scale trials," said lead study author Amit Khera, MD, a former member of the Rader lab who is now completing his residency at the Brigham and Women's Hospital. "The assays we used to measure HDL function are robust and reproducible, thus potentially useful in the early clinical screening of new HDL-targeted therapies to understand how/if they might work."

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