スタディの結果HDL増加はLDL降下に勝る

ARBITER 6-HALTS：スタチンを内服している患者においてナイアシンを用いてHDLを増加させることにより、エゼチミブでLDLを低下させるよりも頸動脈内中膜厚が減少することが示された

ARBITER 6-HALTS: In patients on statins, raising HDL with niacin decreases carotid intima-media thickness more effectively than reducing LDL with ezetimibe

スタチンに高密度リポ蛋白(HDL)コレステロール上昇作用のあるナイアシンを併用させることにより、低密度リポ蛋白(LDL)コレステロール低下作用のあるエゼチミブを併用するよりも動脈壁プラーク蓄積の減少および心疾患リスク低下には有効であることが、2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表され、New England Journal of Medicineに掲載された。コレステロール低下の治療効果に関する研究の血管生物学：動脈硬化に対するHDLおよびLDL治療戦略(The Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6: HDL and LDL Treatment Strategies in Atherosclerosis [ARBITER 6-HALTS])スタディは、動脈硬化性心血管疾患のハイリスク患者363人を組み入れた。対象者は通常のスタチンに加えナイアシンまたはエゼチミブを内服する群に無作為に割り付けられた。一次エンドポイントは頸動脈内中膜厚(IMT)であった。一次エンドポイントが達成されたためスタディは6月に早期終了された。特に、208人の14週間の経過観察データの結果, ナイアシン群においては平均HDLコレステロールが42mg/dLから50mg/dLに上昇し、IMTの有意な減少が認められた。エゼチミブ群においては平均LDLコレステロールレベルが83mg/dLから66mg/dLに低下した。しかし、平均IMTの全般的な変化は認められなかった。

Full Text

In combination with statins, adding a medication that raises high-density lipoprotein (HDL) cholesterol was more effective in reversing artery wall plaque buildup and in reducing heart disease risk than adding a drug that lowers low-density lipoprotein (LDL) cholesterol, researchers reported today at the American Heart Association Scientific Sessions 2009.

In the study titled The Effect of Extended-release Niacin or Ezetimibe Added to Chronic Statin Therapy On Carotid Intima Media Thickness (ARBITER 6-HALTS), researchers found:

- Adding the cholesterol drug niacin to a statin improved HDL cholesterol levels and significantly reduced arterial plaque buildup within 8 months, with further improvement seen at the end of the study (14 months).
- A second approach, adding ezetimibe to a statin, lowered LDL cholesterol to a greater extent, but did not raise HDL. With it, there was no overall effect on arterial build up in the neck arteries.
- With ezetimibe, greater reductions in LDL cholesterol paradoxically were associated with more arterial buildup, a result opposite to that expected.
- The incidence of major cardiovascular events such as fatal and non-fatal heart attack was higher in the ezetimibe group as compared to the niacin group (5 percent vs. 1 percent).

HDL And LDL Treatment Strategies (HALTS) was a prospective, randomized, parallel group, open-label, blinded endpoint study conducted at Walter Reed Army Medical Center in Washington, D.C., and Washington Adventist Hospital in Tacoma Park, Md. It included 363 adults (80 percent male, average age 68 years) with or at high risk for atherosclerotic cardiovascular disease.

All participants were on cholesterol-lowering statin drugs, and their LDL cholesterol was at the treatment goal of under 100 milligrams per deciliter (mg/dL) of blood. Their HDL cholesterol was lower than 50 mg/dL for men and 55 mg/dL for women.

The researchers randomly assigned the subjects to receive either niacin or ezetimibe in addition to their usual statin. The primary endpoint was the change in the wall thickness of the carotid artery in the neck between the two groups of patients. In June, researchers halted the trial early because the primary endpoint was met. Specifically, 14-month follow-up data on 208 patients showed that in the niacin group, average HDL cholesterol rose from 42 mg/dL to 50 mg/dL and there was a significant regression in artery wall thickness. In the ezetimibe group, average LDL cholesterol levels dropped from 83 mg/dL to 66 mg/dL; however no overall change was found in average artery wall thickness.

"These findings for ezetimibe are counter to the prevailing understanding of LDL cholesterol - that lowering LDL cholesterol results in slowing of the atherosclerotic process as has been convincingly shown for other classes of lipid modifying drugs, such as statins and bile acid resins," said Allen J. Taylor, M.D. FAHA, principal investigator of the study and director of Advanced Cardiovascular Imaging and the Lipid/Prevention Clinic in the Department of Medicine (Cardiology) at Washington Hospital Center in Washington, D.C.

In earlier studies demonstrating the protective effects of statins, researchers found strong associations between LDL cholesterol reduction and the prevention of cardiovascular disease. Consequently, many people now view LDL cholesterol reduction as a way to measure whether a treatment will be useful.

But HALTS researchers' findings "challenge the use of LDL reduction as a guaranteed surrogate for clinical performance, particularly for new clinical compounds, and in this particular case, ezetimibe," Taylor said. Patients should know their HDL numbers and, if they are low, ask their doctors if adding a treatment such as niacin is right for them once their LDL is treated to goal with a statin drug, he said.

Co-authors are: Todd C. Villines, M.D.; Patrick J. Devine, M.D.; Mark Turco, M.D.; Len Griffen, M.D.; Michael Miller, M.D.; Eric J Stanek, Pharm. D.; and Neil J Weissman, M.D.

Study sponsor: Abbott Inc. (initially Kos Pharmaceuticals, Inc., Cranbury, N.J.) provided an unrestricted, investigator-initiated research grant administered by the Henry M. Jackson Foundation for the Advancement of Military Medicine in Rockville, Md. The investigators were solely responsible for all aspects of the study and the final decisions on manuscript content.

Disclosures: Dr. Taylor reports receiving lecture fees from Abbott. Dr. Turco reports receiving consulting and lecture fees from Abbott Cardiovascular. Dr. Miller reports receiving lecture fees and grant support from Merck-Schering Plough. Dr. Villines reports receiving lecture fees from Novartis Pharmaceuticals. Dr. Devine reports receiving consulting fees from Medacorp, MDLinx, and Guidpoint Global, equity ownership in Evergreen solar, Openwave, Unifi, Novavax, Genaera Pharm, and Generex Biotech. Dr. Stanek is senior director of research in Personalized Medicine Research and Development at Medco Health Solutions, Inc. (Franklin Lakes, N.J.), but all work performed on this trial was independent of this relationship. No other potential conflict of interest was reported.

Cardiology特集

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