HDLコレステロール薬は心疾患患者のリスクを低下させない（LBCT-19889）

dal OUTCOMES:DalcetrapibはHDLコレステロールを増加させるが心血管イベント再発リスクは減少させないようである

dal OUTCOMES: Dalcetrapib increases HDL-cholesterol but does not appear to reduce risk of recurrent cardiovascular events

心筋梗塞（MI）を発症して間もない患者または狭心症で入院した患者において、高密度リポ蛋白（HDL）コレステロールレベルを上昇させる薬剤は心血管イベント再発リスクを軽減できなかったとのLate-Breaking Clinical Trialの結果が2012年American Heart Association学会において発表され、同時に*New England Journal of Medicine*に掲載された。Effects of Cholesteryl Ester Transfer Protein Inhibitor Dalcetrapib in Patients with Recent Acute Coronary Syndrome（dal OUTCOMES）トライアルにおいて研究者らは、27か国45歳以上の患者15,871人を1日600mgのdalcetrapibまたはプラセボを内服する群に無作為に割り付けた。97%の患者がアスピリンおよびスタチンを内服しており、87%はβ遮断薬を内服していた。平均追跡期間31か月後に、dalcetrapibはHDLコレステロールを約30%上昇させた。しかし、この薬剤は死亡、MI再発、心原性胸痛による入院、または脳卒中を減少させなかった。性別、年齢、喫煙の有無、内服歴、地理的位置またはボディーマスインデックスなどの因子は、この結果に影響しなかった。LDLコレステロールや他の心血管リスクファクターを低下させる薬剤を既に内服している患者においてHDLコレステロールが依然として重要な因子かどうかは疑問であると研究者らは述べている。

Full Text

Among patients who had a recent myocardial infarction (MI) or hospitalization for angina, a drug that boosts high-density lipoprotein (HDL) cholesterol levels failed to reduce the risk of further cardiovascular events, according to a late-breaking clinical trial presented at the American Heart Association's Scientific Sessions 2012.

The Effects of the Cholesteryl Ester Transfer Protein Inhibitor Dalcetrapib in Patients with Recent Acute Coronary Syndrome (dal OUTCOMES) is also published in the *New England Journal of Medicine*.

Dalcetrapib increased levels of HDL cholesterol by about 30 percent. However, among nearly 16,000 patients followed for an average of about 2 ½ years, this HDL cholesterol boost didn't reduce patients' risk of death, another MI, hospitalization for heart-related chest pain, or stroke.

Researchers ended the study in May, when an interim analysis showed that the drug neither provided the expected benefit, nor caused harm.

Many studies have shown that low levels of HDL in the bloodstream are associated with a higher risk of heart disease and stroke. However, the role, if any, for drugs that raise HDL is less certain. "Sometimes a study advances scientific knowledge even though it does not advance therapeutic options," said Gregory Schwartz, M.D., Ph.D., lead study author. "I believe this study did just that by providing an unexpected answer to an important scientific question."

Dalcetrapib is a cholesteryl ester transfer protein (CETP) inhibitor. Drugs in this class block the transfer of cholesterol from HDL to low-density lipoprotein (LDL), thereby raising the levels of HDL in the bloodstream.

Researchers will undoubtedly debate why the treatment didn't work, which may have a bearing on other drugs in the CETP class that remain under investigation, said Schwartz, chief of the Cardiology Section at Denver VA Medical Center and Professor of Medicine at the University of Colorado in Denver.

Most of the patients studied were also being treated with statin drugs, as well as other medications to reduce risk after MI, such as aspirin, clopidogrel, and beta-blockers.

"It's possible that when patients are treated with all these risk-reducing drugs, HDL cholesterol level is no longer a risk factor," said Schwartz. "It's also possible that HDL is protective in healthy persons, but is altered in patients with heart disease so that it no longer serves the same protective function. Or, it may be that the specific way that dalcetrapib raises HDL is not advantageous."

Researchers randomly assigned 15,871 patients age 45 and older in 27 countries to take either 600 milligrams of dalcetrapib or a placebo daily. Ninety-seven percent also took aspirin and statins, and 87 percent took beta-blockers to reduce the risk of heart complications.

Launched in 2008, the study had average follow-up of 31 months. Although patients taking dalcetrapib had higher HDL levels, 8.3 percent had a major cardiovascular event, compared with 8 percent of the placebo group. Factors such as gender, age, smoking status, medical history, geographical location or body mass index didn't influence the results, researchers said.

More research is needed to better understand how HDL functions in healthy people compared with patients who have cardiovascular disease, and to learn how CETP inhibitors affect the composition and function of HDL.
In the meantime, there has been no medicine to date that has shown improved outcomes by raising HDL in patients such as these.

"Perhaps the focus should be not so much on raising the level of HDL cholesterol, but on modifying or eliminating the risk factors that are associated with low HDL cholesterol, such as smoking, obesity, diabetes, and sedentary lifestyle."
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