スタチン療法にエゼチミブを併用することで臨床上の有益性が得られる (Abstract 20742)

IMPROVE-IT：異なる作用のコレステロール低下療法はスタチンの心血管リスク低下を増強する

IMPROVE-IT : Cholesterol-lowering drug with different action adds to statin's reduction of cardiovascular risk

高リスクの急性冠症候群（ACS）患者においてスタチン療法に他のタイプのコレステロール低下薬を併用することにより心筋梗塞（MI）および脳卒中がより予防できる、との大規模長期スタディが2014年American Heart Association年次集会で発表された。IMPROVE-IT（IMProved Reduction of Outcomes: Vytorin Efficacy International Trial）スタディは、低比重リポ蛋白（LDL）コレステロールレベルが125mg/dL以下、または既にスタチン内服中であれば100mg/dL以下の50歳以上のACS患者18,144人を組み入れた。患者は平均約6年間追跡され、長期の者では8.5年であった。シンバスタチンとプラセボを投与された患者と比較し、シンバスタチンと非スタチン系薬剤エゼチミブの両者を投与された患者は、全ての心血管イベントリスクが6.4%、MIリスクが14%、脳卒中リスクが14%、および虚血性脳卒中リスクが21%低かった。心血管疾患死は両群ともに統計学的に同等であった。IMPROVE-ITはスタチン療法に非スタチン系薬剤を併用した際の著明な臨床上の有益性を示した初めてのスタディである。

Full Text

Adding another type of cholesterol-lowering drug to statin therapy can better prevent myocardial infarction (MI) and strokes in high-risk patients with acute coronary syndrome (ACS), according to a large, long-term study presented at the American Heart Association's Scientific Sessions 2014.

Compared to patients with coronary heart disease given the drug simvastatin plus a placebo, those given both simvastatin and the non-statin drug, ezetimibe, had a 6.4 percent lower risk of all cardiovascular events, a 14 percent lower risk of all heart attacks, a 14 percent lower risk of stroke, and a 21 percent lower risk of ischemic stroke. Deaths from cardiovascular disease were statistically the same in both groups. Patients were followed an average of approximately six years, and some as long as 8.5 years. Approximately 2 patients out of every 100 patients treated for 7 years avoided a heart attack or stroke. (Number Needed to Treat (NNT) = 50).

"The study is the first to show that adding another non-statin drug to a statin to improve cholesterol levels can help patients with specific heart problems do better," said Christopher P. Cannon, M.D., lead author and a professor of medicine at Harvard Medical School and physician at Brigham and Women's Hospital.

The study, called IMPROVE-IT (IMProved Reduction of Outcomes: Vytorin Efficacy International Trial), was done at 1,158 centers in 39 countries. It enrolled 18,144 patients with ACS 50 years or older with low-density lipoprotein (LDL) cholesterol levels at or less than 125 mg/dL, or at or less than 100 mg/dL if they were already using a statin.

"The patients, enrolled within 10 days of hospitalization for a heart attack or unstable angina, were high risk," Cannon said. About 5,000 of them had suffered a ST-segment elevation myocardial infarction, or STEMI. The remaining 13,000 had suffered a non-STEMI heart attack or had unstable angina. Patients also had at least one feature putting them at high risk for a further cardiovascular event, including a previous MI, diabetes, peripheral artery or cerebrovascular disease, coronary disease in multiple arteries, or bypass surgery in the past.

Statins, such as simvastatin, block cholesterol production in the liver, while ezetimibe, a cholesterol absorption inhibitor, reduces the body's absorption of cholesterol in the intestine. In the study, the dual therapy reduced patients LDL to an average of 54 mg/dL, compared with 69 for those treated with the statin and placebo.

"We took those patients from a clinically appropriate target LDL-C to even lower. We now have solid evidence that lower is good, and even lower can be even better," he said.

The addition of ezetimibe did not raise patients risk of ill effects, such as liver or muscle problems, or cancer, Cannon said.
Over a decade ago, researchers from the TIMI Study Group, based at Brigham and Women's Hospital demonstrated that a high dose statin, which lowered cholesterol further than a regular dose statin, provided better clinical outcomes. But questions remained about whether further reducing cholesterol would be even more effective in reducing cardiovascular-related events. And now, researchers have an answer from the results of the IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT).

Co-authors include study chairmen Eugene Braunwald, M.D., and Robert Califf, M.D., on behalf of the IMPROVE-IT investigators.

"These study results will help expand our treatment options for high-risk ACS patients, especially among those who are intolerant of or who do not achieve desired results with intense statin therapy," said Lori Mosca, M.D., M.P.H., Ph.D., and Professor of Medicine at Columbia University Medical Center and Director of Preventive Cardiology at New York-Presbyterian Hospital. "These results are consistent with decades of research in high-risk ACS patients affirming the central role of aggressive LDL reduction in the prevention of recurrent heart disease. They further suggest that we should consider setting the LDL bar even lower among our high-risk patients to achieve maximum benefit to prevent recurrent heart disease and stroke," Mosca continued.

"Science by nature is evolutionary. Each piece of new data advances our understanding of how to prevent, detect, diagnose and treat heart disease," said Elliott Antman, M.D., President of the American Heart Association. "We are learning more about the biology of cardiovascular disease, and we are making progress."

The IMPROVE-IT study was funded by a research grant from Merck & Co.

Cardiology特集

AHA2014 (第87回米国心臓病協会)

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