糖尿病患者におけるアテロームの成長（LBCT, abstract＃5221）

APPROACH Trial：心血管疾患を有する糖尿病患者においてrosiglitazoneは動脈硬化の進行に影響しないようである

APPROACH Trial: Rosiglitazone does not appear to affect progression of atherosclerosis in diabetics with cardiovascular disease

Rosiglitazone(RSG)―チアゾリジンディオンクラスの糖尿病治療薬の一種―は、glipizideとの比較試験において冠動脈のアテロームの成長を軽減するとの一次エンドポイントに合致しなかったと2008年American Heart Association学会で発表された。APPROACHトライアル―心血管疾患の既往を有する2型糖尿病患者におけるrosiglitazoneによる動脈硬化の進行予防に対する評価―の結果がLate-Breaking Clinical Trialとして発表された。計672人の患者が19ヵ国92の医療機関での、冠動脈疾患を有する糖尿病患者を対象とした世界で最も大規模な血管内超音波（IVUS）二重盲検試験に組み入れられ無作為化された。治療18ヵ月後のアテローム容積変化率はRSGを投与された患者においてglipizideを投与された患者と比較し、統計学的な有意差はなかった（p=0.12）。二次アウトカムにおいてRSG群では標準化総アテローム容積の有意な減少（p=0.04）および最もアテロームの多い10mmのアテローム容積の有意ではない減少（p=0.13）を認めた。あらかじめ規定したサブグループ解析から、rosiglitazoneはより進行した糖尿病患者において抗動脈硬化効果がより認められるとの仮説がかかげられた。

Full Text

Rosiglitazone - a member of the thiazolidinedione class of diabetes drugs - did not meet its primary endpoint for reducing progression of atheroma in coronary arteries in a study comparing it with glipizide, according to research presented at the American Heart Association's Scientific Sessions 2008. Results of The APPROACH Trial - Assessment on the Prevention of Progression by Rosiglitazone on Atherosclerosis in Type 2 Diabetes Patients with Cardiovascular History were presented as a late-breaking clinical trial.

In the world's largest intravascular ultrasound (IVUS) study of diabetic patients with established coronary artery disease, researchers sought to determine if the choice of diabetes drugs could affect the progression of atherosclerosis as measured by IVUS, said Richard W. Nesto, M.D., Ph.D., principal investigator of the study, an associate professor of cardiovascular medicine at Lahey Clinic in Burlington, Mass., and chair of the division of internal medicine at Brigham and Women's Hospital in Boston.

The prospective, randomized, double blind study followed 672 diabetic patients, average age 61, undergoing clinically necessary coronary angiography or percutaneous coronary intervention (PCI) at 92 medical centers in 19 countries.

During those procedures, the researchers used IVUS to measure plaque burden in a 40 mm segment of a non-intervened artery with atherosclerosis at a level considered too low to require treatment. The participants were then randomized to one of the two study drugs with dosages adjusted to achieve similar levels of glucose control in each group.

After 18 months of treatment, the 333 patients receiving RSG had high-density lipoprotein (HDL) levels of 49 milligrams per deciliter (mg/dL), nearly 8 percent higher than the 45.4 mg/dL level in the 339 patients randomized to glipizide.

Researchers also found beneficial directional effects on blood pressure, triglycerides and hs-CRP in the rosiglitazone group and also a modest increase in low-density lipoprotein (LDL) of 2.8 mg/dL.

At the end of the treatment period, researchers performed a second IVUS to determine the study's primary endpoint, defined as the change in percentage of atheroma in the segment of non-intervened artery. They found that RSG seemed to stall or possibly reverse atherosclerotic progression with a 0.21 percent reduction in the primary outcome of percentage of plaque volume in RSG patients, compared to a 0.43 percent increase in plaque in glipizide patients. This difference in drug effect did not achieve statistical significance. However, researchers found a significant 5.12 millimeter cubed (mm^3) decrease in normalized total atheroma volume in favor of the RSG group.

Researchers found no statistically significant differences in the secondary endpoint of major cardiovascular events between groups, although the study was not powered to evaluate clinical outcomes, he said. They did find statistically significant differences in adverse events with 28 percent of participants taking glipizide experiencing a low-blood-sugar incident compared to 8 percent of those in the RSG group. In addition, the RSG group had multiple measures indicating fluid retention, although there was no difference in the risk of congestive heart failure.

Results from the APPROACH trial are in line with similar and statistically significant results from an earlier, slightly smaller PERISCOPE trial, which used two different diabetes drugs - pioglitazone and glimepiride - from the same two classes, Nesto said.

The mechanism is probably multifactorial by affecting several cardiovascular risk factors, one of which may be raising the levels "good" cholesterol by nearly 8 percent.

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