

ワルファリンより安全な代替療法

ACTIVE-A: 大血管イベントの予防に関してクロピドグレル／アスピリンの併用はワルファリンよりも安全な代替療法の方法である

ACTIVE-A: Clopidogrel/aspirin combination therapy appears to be a safer alternative to warfarin for prevention of major vascular events

クロピドグレルとアスピリンの併用により大血管イベントが11%減少したとのレイトブレイキングクリニカルトライアルACTIVE-Aの結果が、2009年第58回American College of Cardiology学会で発表された。2006年には、クロピドグレルをアスピリンに追加してもワルファリンよりも有効性が低いとのACTIVE-Wの結果が報告されたが、このスタディに参加した患者の多くはスタディに組み入れられた時点でワルファリンをすでに内服していたため、ワルファリンに好ましいバイアスがかかっていた可能性があり、この結果は解釈が難しかった。ACTIVE-Aでは、心房細動の認められた患者7,554人に対してアスピリンにクロピドグレルを併用投与した効果を、二重盲検プラセボコントロール試験で直接評価した。このトライアルでは全ての患者がアスピリン（推奨用量：一日75～100mg）を内服しており、クロピドグレル（一日75mg）またはプラセボを内服する群に無作為に割り付けられた。主要な血管イベント全体（脳卒中、心筋梗塞、中枢神経系以外の全身性塞栓症または血管死の合計）の発現が11%低下したのに加え、併用療法の結果、脳卒中発現率が28%低下し心筋梗塞発現率が23%低下した。クロピドグレルにより年1.27～2%であった重大な出血のリスクが58%増加した。

Full Text

A combination of clopidogrel and aspirin reduces major vascular events by 11 percent, including a 28 percent reduction in stroke and a 23 percent reduction in myocardial infarction, according to research presented at the American College of Cardiology's 58th annual scientific session.

The results of ACTIVE-A assessed the safety and efficacy of adding clopidogrel to aspirin in high-risk atrial fibrillation (AF) patients who are unsuited to use vitamin K antagonists (VKA) such as warfarin as a treatment therapy for AF.

Oral anticoagulants, such as warfarin and aspirin, are the only proven effective therapies in treatment for AF, and warfarin has proved to be the more effective of the two. However, many patients who are unsuited to use VKA such as warfarin, and they receive aspirin. Warfarin reduces stroke by 38 percent; however, it increases major hemorrhage by 70 percent and intracranial hemorrhage by greater than 100 percent. It is also difficult to tolerate, requiring monitoring and restrictions of lifestyle. Aspirin alone is modestly effective, reducing stroke by 22 percent.

Guidelines recommend warfarin for high-risk patients but many patients do not take it because of bleeding risk or because of their physician does not recommend it.

"The purpose of the ACTIVE-A trial was to determine if the addition of clopidogrel to aspirin would reduce major vascular events and stroke in patients with AF, at an acceptable risk of increased hemorrhage," said Stuart Connolly, M.D. of McMaster University and one of the principle investigators of ACTIVE-A. "If you treated one thousand patients over the course of three years by adding clopidogrel to aspirin, you would prevent 28 strokes, 17 of which would be fatal or disabling, and you would prevent six heart attacks. This would occur at a cost of 20 major hemorrhages."

In 2006, the ACTIVE-W study reported that adding clopidogrel to aspirin was less effective than warfarin, but this result is difficult to interpret because most patients in that study were on warfarin at the time of enrollment, potentially biasing results in favor of warfarin. In ACTIVE-A the effect of adding clopidogrel to aspirin is directly evaluated in a double-blind placebo-controlled clinical trial of 7,554 patients with documented AF and at least one risk factor for stroke.

In ACTIVE-A, all patients were treated with aspirin (75-100 mg/day, recommended) and randomized to receive either clopidogrel (75 mg/day) or matching placebo. The primary outcome was the composite of stroke, myocardial infarction, non-CNS systemic embolus or vascular death; major bleeding was a secondary safety outcome. Clopidogrel increased risk of major hemorrhage by 58 percent from 1.27 percent to 2 percent/year.

"Addition of clopidogrel to aspirin in many patients with AF, unsuitable for warfarin will provide an overall benefit at an acceptable risk," said Salim Yusuf, M.D. of McMaster University and one of the principle investigators "When compared to aspirin alone, warfarin is more effective than clopidogrel plus aspirin against stroke in AF. However clopidogrel provides only about three-quarters of the benefit of warfarin over aspirin, but with only about three-quarters of the increased risk of major and intracranial hemorrhage."

ACC2009特集

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