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My patient had a small vessel stroke, are two antiplatelet agents better than one?

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Why is this study of clinical importance?

Small subcortical brain infarcts, commonly known as lacunar strokes, constituteabout 25% of ischaemic strokes. Aspirin is accepted as a standard antiplatelet therapy in patients with lacunar infarcts. Dual Antiplatelet therapy has been associated with increased bleeding, although it has been shown to reduce the risk of stroke among patients with atrial fibrillation.

The SPS3 trial was a randomized, multicenter clinical trial conducted in 82 clinical centers inNorth America, Latin America, and Spain. It tested two randomized interventions, in a 2-by-2 factorial design, in patients with MRI-confirmed lacunar stroke: clopidogrel and aspirin versus aspirin alone and two target levels of systolic blood pressure (<130 mm Hg vs. 130 to 149 mm Hg).

This trial was not pharmaceutically sponsored. It was an investigator initiated trial. The final results of the antiplatelet component of the trial have now been published.

Who were the participants?

Between 2003 and 2011, a total of 3020 patients were enrolled in the study: 1503 in the group treated with aspirin plus placebo and 1517 in the group treated with aspirin plus clopidogrel.

Patients were eligible for participation in the study if they were 30 years of age or older, had undergone a symptomatic lacunar stroke within the preceding 180 days, and did not have surgically amenable ipsilateral carotid artery disease or cardioembolism.

What was the intervention?

In accordance with the 2-by-2 factorial design of the study, eligible patients underwent simultaneous randomization to the antiplatelet intervention (in which both patients and practitioners were unaware of group assignments) and to one of the two groups defined by target levels for systolic blood pressure (<130 mm Hg vs. 130 to 149 mm Hg) (with patients and practitioners aware of the group assignments).

All participants were given 325 mg of enteric-coated aspirin daily and were randomly assigned to receive 75 mg of clopidogrel daily or a matching placebo, with adherence measured by means of pill counts performed at quarterly follow-up visits.

What are the results?

The participants had a mean age of 63 years, and 63% were men. After a mean follow-up of 3.4 years, the risk of recurrent stroke was not significantly reduced with aspirin and clopidogrel (dual antiplatelet therapy) (2.5% per year) as compared with aspirin alone (2.7% per year) (hazard ratio, 0.92; 95% confidence interval [CI], 0.72 to 1.16), nor was the risk of recurrent ischaemic stroke (hazard ratio, 0.82; 95% CI, 0.63 to 1.09) or disabling or fatal stroke (hazard ratio, 1.06; 95% CI, 0.69 to 1.64). The risk of major haemorrhage was almost doubled with dual antiplatelet therapy (105 haemorrhages, 2.1% per year) as compared with aspirin alone (56, 1.1% per year) (hazard ratio, 1.97; 95% CI, 1.41 to 2.71; P<0.001).

What were the conclusions?

Among patients with recent lacunar strokes, the addition of clopidogrel to aspirin did not significantly reduce the risk of recurrent stroke and did significantly increase the risk of bleeding and death.

How does this impact us?

In Pakistan there is a high prevalence of Diabetes mellitus and Hypertension which frequently causes lacunar stroke. It appears from this trial, that at least in Lacunar strokes, two agents (aspirin and clopidrogel) are not better than one. In addition, given the lifelong nature of therapy after stroke, this data will assist in reducing prescription costs in a resource poor nation.

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Recommended Reading

1. SPS3 Investigators. Benavente OR, Hart RG, McClure LA, Szychowski JM, Coffey CS, Pearce LA. Effects of clopidogrel added to aspirin in patients with recent lacunar stroke. N Engl J Med 2012; 367: 817-25.