

Ticlopidine was not better than aspirin for preventing recurrent stroke in African-Americans with noncardioembolic ischemic stroke

Gorelick PB, Richardson D, Kelly M, et al. Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial. *JAMA*. 2003;289:2947-57.

QUESTION

In African-American patients with noncardioembolic ischemic stroke, is ticlopidine more effective than aspirin for preventing recurrent stroke?

DESIGN

Randomized (allocation concealed*), blinded (clinicians, data collectors, outcome assessors, and data analysts),* placebo-controlled trial with 2-year follow-up (African American Antiplatelet Stroke Prevention Study [AAASPS]).

SETTING

62 academic and community hospitals in the United States.

PATIENTS

1809 African-American patients 29 to 85 years of age (mean age 61 y, 53% women), who had noncardioembolic ischemic stroke onset ≥ 7 but not ≥ 90 days, cranial computed tomography or magnetic resonance imaging of the brain consistent with the entry cerebral infarction, measurable neurologic deficit that correlates with entry cerebral infarction, and availability for follow-up in an outpatient treatment program. Exclusion criteria included transient ischemic attack, subarachnoid hemorrhage, cardiac source embolism, iatrogenic stroke, nonatherosclerotic stroke, postoperative stroke occurring

within 30 days of operation, and carotid endarterectomy as primary treatment measure for entry cerebral infarction. All patients were included in the analysis.

INTERVENTION

Patients were stratified by site and allocated to ticlopidine, 250 mg with placebo aspirin tablet twice daily with meals ($n = 902$), or aspirin, 325 mg with placebo ticlopidine tablet twice daily with meals ($n = 907$).

MAIN OUTCOME MEASURES

A composite endpoint of recurrent stroke, myocardial infarction (MI), or vascular death (death caused by ischemic or hemorrhagic stroke, MI, sudden death, pulmonary embolism, heart failure, visceral or limb infarction, or a vascular procedure or operation). Secondary outcomes included incidence of recurrent stroke or death, nonfatal or fatal stroke, recurrent stroke, MI, or death from all causes.

MAIN RESULTS

Analysis was by intention to treat. Ticlopidine and aspirin groups did not differ for the composite endpoint of recurrent stroke, MI, or vascular death (Table); secondary outcomes; or overall adverse events (29.9% vs 28.9%). The study had 80% power to detect a 25% relative risk reduction in the 2-year primary event rate.

CONCLUSION

In African-American patients with noncardioembolic ischemic stroke, ticlopidine was not better than aspirin for preventing recurrent stroke.

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*See Glossary.

Ticlopidine vs aspirin for noncardioembolic ischemic stroke at 2 years†

Outcome	Ticlopidine	Aspirin	RRI (95% CI)	NNH
Composite endpoint	15%	12%	20% (-6 to 52)	Not significant

†Composite endpoint = recurrent stroke, myocardial infarction (MI), or vascular death (ischemic or hemorrhagic stroke, MI, sudden death, pulmonary embolism, heart failure, visceral or limb infarction, or a vascular procedure or operation). Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article using Cox proportional-hazards model.

COMMENTARY

In studies of stroke prevention, results for whites may not be directly generalizable to African-Americans. The burden of stroke is greater among African-Americans than whites, and this may be explained by an uneven distribution of known risk factors (e.g., hypertension and diabetes), disparities in how well these risk factors are treated, genetic and other unidentified risk factors, or the distribution of stroke subtypes. Despite these important racial differences, African-Americans have not been well represented in trials of stroke prevention.

AAASPS, the first large-scale trial of secondary stroke prevention to focus on African-Americans, was prompted in part by the encouraging results from a subgroup analysis of the Ticlopidine Aspirin Stroke Study (TASS) (1). In TASS, ticlopidine showed a greater benefit for preventing stroke and other vascular events compared with aspirin and was associated with fewer adverse events among African-Americans than whites. The effect was large enough (24% relative risk reduction in stroke or death) to justify another trial.

Regrettably, AAASPS failed to confirm the results of TASS: Ticlopidine was no more effective than aspirin for preventing recurrent stroke, MI, or vascular death. Because ticlopidine is expensive and is associated with infrequent but serious adverse events such as thrombo-

cytopenia and neutropenia, little justification exists for using it to prevent recurrent stroke in African-Americans who can tolerate aspirin.

Clopidogrel has largely replaced ticlopidine as the nonaspirin antiplatelet agent of choice for the prevention of stroke and cardiovascular events because it is associated with fewer major adverse events. Although clopidogrel is a treatment option for patients who cannot tolerate aspirin, AAASPS does not support its preferential use in African-Americans.

Although the AAASPS was a negative trial, it should be seen as a success. It dispels myths about the infeasibility of recruiting minority populations and underlines the importance of specifically studying these groups. The recruitment methods used in the AAASPS are likely to be copied repeatedly in the future.

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Reference

1. Weisberg LA. The efficacy and safety of ticlopidine and aspirin in non-whites: analysis of a patient subgroup from the Ticlopidine Aspirin Stroke Study. *Neurology*. 1993;43:27-31.