Aspirin is an antiplatelet agent used in low doses (75-100 mg/d) to prevent cardiovascular events. It is still widely used for primary and secondary prevention of stroke, despite some recent unfavorable findings. The increasing bleeding tendency is its major adverse effect. In this prospective, randomized, double-blind, placebo-controlled trial (The Aspirin in Reducing Events in the Elderly- ASPREE), the authors from Australia and the United States evaluated the risk of ischemic stroke and intracranial hemorrhage in a cohort of nearly 20,000 older people who were free of overt cardiovascular disease and were treated with long-term, daily, low-dose aspirin.



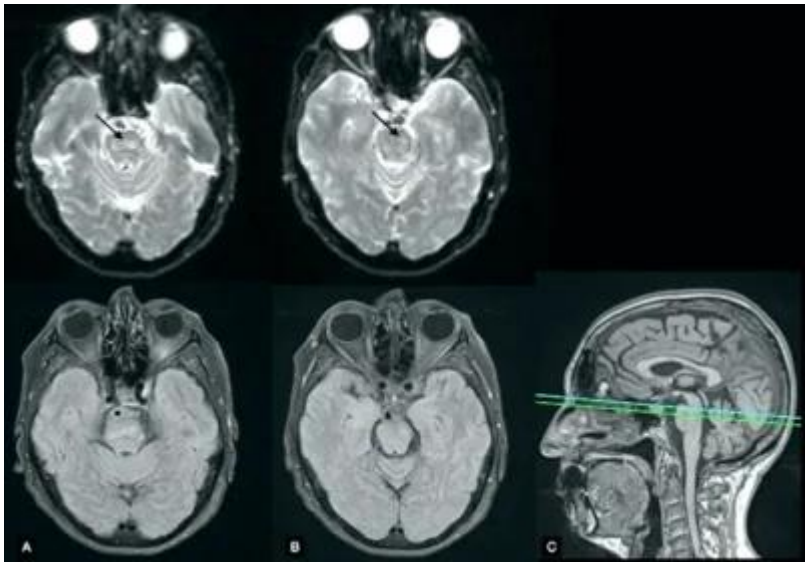
About the study

The Aspirin in Reducing Events in the Elderly (ASPREE) trial was a prospective, randomized, double-blind, placebo-controlled trial that evaluated the administration of daily low-dose aspirin in older adults without overt cardiovascular disease. The study conducted in Australia and the United States included individuals who were 70 years of age or older and who did not have a history of atrial fibrillation, stroke, transient ischemic attack, or myocardial infarction. No participants were diagnosed with dementia or physical disability.

Participants were randomized and assigned to receive daily 100 mg enteric-coated aspirin or a matching placebo. Median follow-up was 4.7 years, ranging from 3.6 to 5.7 years.

The researchers provided a comprehensive report on the incidence of the first stroke or bleeding events during the follow-up. The ischemic strokes were categorized into four groups: a) cardioembolic (a clear cardiac cause, typically atrial fibrillation), b) large-vessel atherosclerosis (ischemic stroke with ≥50% of extracranial or intracranial stenosis), c) small-vessel occlusion (clinical lacunar stroke syndrome and evidence of a lacunar infarction), and d) undetermined etiology (no cause was identified or etiological investigations were incomplete).

Intracranial hemorrhage was categorized based on the location identified on neuroimaging (basal ganglionic, lobar, brainstem, or other) or as subarachnoid, subdural, or extradural.



Results

The analysis of this clinical trial included 19 114 older adults. 56% were females, and the median age was 74. Out of 19 114 participants, 9525 were treated with aspirin and 9589 received a placebo.

The first stroke was diagnosed in 203 individuals (4.7%) who received a placebo and 195 individuals (4.6%) treated with aspirin. 22% of all strokes (86 cases) were hemorrhagic strokes.

Aspirin treatment did not reduce the risk of ischemic stroke. 146 (1.5%) participants treated with aspirin and 166 individuals (1.7%) assigned to a placebo had the ischemic stroke. There was no evidence of a differential effect of aspirin across subgroups regarding age, sex, smoking, diabetes, dyslipidemia, hypertension, or country (Australia or the USA).

Participants treated with low-dose aspirin (49 individuals, 0.5%) had a similar rate of hemorrhagic stroke as participants who received a placebo (37 individuals, 0.4%). The rates of other intracranial bleeding (subarachnoid, subdural, or extradural) did not differ between participants assigned to aspirin or placebo. However, the totals of intracranial hemorrhage, resulting from a combination of hemorrhagic stroke and other intracranial bleedings, such as subdural, extradural, and subarachnoid bleeding, were significantly more frequent among individuals treated with aspirin than in those assigned to placebo.

The biggest difference in the location of hemorrhagic stroke between groups was within the territory of deep perforator arteries of the basal ganglia, but this difference was not statistically significant.

Conclusion

This study showed the incidence of ischemic stroke did not differ between the participants treated with aspirin and the placebo group, but the totals of intracranial hemorrhage were significantly more frequent among individuals treated with aspirin than in those assigned to placebo.

Head injuries, usually from falls, are common among older people. The authors noted that clinicians should be aware of an increased risk of intracerebral bleeding among older individuals who are treated with aspirin and are prone to falls and head trauma.

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