

Review: Aspirin lowers the risk for MI but not for stroke in persons who do not have established vascular disease

Hart RG, Halperin JL, McBride R, et al. Aspirin for the primary prevention of stroke and other major vascular events. Meta-analysis and hypotheses. Arch Neurol. 2000 Mar;57:326-32.

QUESTION

For persons who do not have clinically recognized vascular disease, is aspirin effective for reducing stroke and other vascular events?

DATA SOURCES

Studies were identified by searching for English-language articles in {MEDLINE}* (1980 to 1998) with the terms clinical trial, aspirin, and stroke; the Cochrane Collaboration Trials Registry; the Antiplatelet Trialists' Collaboration lists of publications; and bibliographies of review articles.

STUDY SELECTION

Studies were selected if they were randomized controlled trials or large observational studies of aspirin in any dose; trials compared aspirin with placebo for primary prevention of stroke; data were provided on persons who did not have established vascular disease at baseline; and outcomes were stroke, myocardial infarction, or other major vascular events.

DATA EXTRACTION

Data were extracted on study population and size, aspirin dose, and outcomes.

MAIN RESULTS

5 randomized controlled trials met the inclusion criteria. 52 251 participants (mean age 57 y, 80% men) were studied, and mean follow-up was 4.6 years. Aspirin and placebo doses were 75 mg/d for 21 330 participants, 325 mg every other day for 22 071 participants, and 500 to 650 mg/d for 8850 participants. Aspirin was associated with a small decreased risk for myocardial infarction and a trend toward decreased all-cause mortality, but it was not associated with decreased risk for stroke, hemorrhagic stroke, or vascular death (Table). The participants' underlying vascular risk or the dose of aspirin used was not related to any outcome.

CONCLUSION

In participants who have no clinical evidence of vascular disease, aspirin reduces the risk for myocardial infarction but does not reduce the risk for stroke or vascular death.

Source of funding: No external funding.

For correspondence: Dr. R.G. Hart, Department of Medicine (Neurology), University of Texas Health Science Center MSC7883, 7703 Floyd Curl Drive, San Antonio, TX 78229-3900, USA. FAX 210-567-4659.

*Information supplied by author.

Aspirin vs placebo for primary prevention of vascular events at mean follow-up of 4.6 years†

Outcomes at mean 4.6 y	Number of studies	Patients	Relative risk (95% CI)	NNT (CI)
Myocardial infarction	5	All	0.74 (0.68 to 0.82)	115 (91 to 164)
All-cause mortality	5	All	0.94 (0.87 to 1.01)	Not significant
Stroke	5	All	1.08 (0.95 to 1.24)	Not significant
Hemorrhagic stroke	4	All	1.35 (0.88 to 2.10)	Not significant
Vascular death	5	All	0.93 (0.93 to 1.03)	Not significant

†Abbreviations defined in Glossary; NNT and CI calculated from data provided by author.

COMMENTARY

According to the analysis by the Antiplatelet Trialists' Collaboration (1), aspirin is effective for the secondary prevention of stroke. Although physicians are often asked whether aspirin should be taken, it remains unclear whether it is beneficial for the primary prevention of stroke or other vascular events. Only 2 large prospective trials of aspirin in healthy men have been completed. Data from the ongoing Women's Health Study (2) will soon provide evidence on the efficacy of aspirin for primary prevention of heart disease and stroke among healthy women.

In this methodologically sound meta-analysis of the 5 existing randomized trials on the subject, Hart and colleagues conclude that aspirin is not beneficial in the primary prevention of stroke among persons with no vascular disease. Indeed, aspirin may increase the risk for stroke, although this trend is not significant. Results of the Physicians' Health Study (3), that aspirin therapy may prevent myocardial infarction among men > 55 years of age who have risk factors for cardiovascular disease, are supported by this systematic review. A nonsignificant trend showed a higher rate of intracranial hemorrhage among persons who use aspirin. Whether intracranial

hemorrhage explains the higher stroke incidence with aspirin use in primary stroke-prevention studies is unclear, but it is a cause for concern. Aspirin should therefore be prescribed for stroke prevention only for patients with vascular disease, particularly those with a history of transient ischemic attack or stroke. For patients who cannot tolerate aspirin, clopidogrel or ticlopidine are effective alternatives.

Richard L. Harvey, MD
Northwestern University Medical School
Chicago, Illinois, USA

References

1. Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy—I: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. BMJ. 1994;308:81-106.
2. Buring JE, Hennekens CH. The Women's Health Study: summary of the study design. J Myocardial Ischemia. 1992;4:27-9.
3. Steering Committee of the Physicians' Health Study Research Group. Final report on the aspirin component of the ongoing Physicians' Health Study. N Engl J Med. 1989;321:129-35.