Review: Aspirin reduces CAD events in persons with no history of cardiovascular disease, but it increases gastrointestinal bleeding

Hayden M, Pignone M, Phillips C, Mulrow C. **Aspirin for the primary prevention of cardiovascular events: a summary of the evidence for the U.S. Preventive Services Task Force.** Ann Intern Med. 2002 Jan 15;136:161-72.

QUESTION

What are the benefits and harms of aspirin use to prevent coronary artery disease (CAD) events in persons with no history of cardiovascular disease?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to May 2001), reviewing bibliographies of relevant studies and systematic reviews, and contacting experts.

STUDY SELECTION

Randomized controlled trials (RCTs) of aspirin-related benefits were selected if they compared aspirin with placebo or no aspirin; included participants with no history of cardiovascular disease; had a duration ≥ 1 year; and assessed myocardial infarction (MI), stroke, and mortality. Case–control studies, RCTs, and systematic reviews of aspirin-related harms were selected if they assessed hemorrhagic stroke or gastrointestinal (GI) bleeding.

DATA EXTRACTION

Data were extracted on duration of treatment, patient characteristics, aspirin dosage, control condition, and additional therapies. Quality of trials was assessed.

MAIN RESULTS

5 RCTs (n = 035) were included in the meta-analysis: the British Male Doctors' Trial, the Physicians' Health Study (PHS), the Thrombosis Prevention Trial (TPT), the Hypertension Optimal Treatment Trial, and the Primary Prevention Project. Most participants were men (78%) and were middle-aged, and aspirin dosage was ≤ 162 mg/d in 4 trials and 500 mg/d in 1 trial. Study quality was high overall. Meta-analyses showed that aspirin reduced the combined outcome of nonfatal MI or death from CAD but did not differ from the control intervention for CAD mortality alone, all-cause mortality, or stroke (Table). Previous meta-analyses that included the 5 trials showed that aspirin increased therisk for a major GI bleeding event but did not differ from the control intervention for hemorrhagic stroke (Table).

CONCLUSIONS

In persons with no history of cardiovascular disease, aspirin reduces the risk for overall coronary artery disease events but does not affect the risk for CAD mortality, all-cause mortality, or stroke. The risk for gastrointestinal bleeding is increased, but the risk for hemorrhagic stroke is not.

Source of funding: Agency for Healthcare Research and Quality.

For correspondence: Dr. M. Pignone, University of North Carolina Hospital, Chapel Hill, NC, USA. E-mail pignone@med.unc.edu.

Aspirin vs the control intervention for prevention of coronary artery disease (CAD) events in persons with no history of cardiovascular disease*

Outcomes at 3 to 7 y	Weighted event rates		RRR (95% CI)	NNT (CI)
	Aspirin	Control		
Total coronary events	1.9%	2.4%	28% (13 to 39)	150 (105 to 324)
CAD mortality	0.67%	0.63%	13% (–9 to 30)	Not significant
All-cause mortality	3.5%	3.4%	7% (–2 to 16)	Not significant
			RRI (CI)	NNH (CI)
Stroke	1.4%	1.3%	2% (–15 to 23)	Not significant
Major gastrointestinal bleeding†	0.8%	0.48%	69% (40 to 109)	302 (193 to 528)
Hemorrhagic stroke†	0.22%	0.17%	40% (–10 to 100)	Not significant

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article by using a random-effects model.
†Calculated from data in Sudlow C. What is the role of antithrombotic treatment in asymptomatic people? In: Barton S, ed. Clinical Evidence, Issue 5. London: BMJ Publishing Group; 2001:93.

COMMENTARY

The meta-analysis by Hayden and colleagues provides the rationale behind the recent U.S. Preventive Services Task Force (USPSTF) recommendation supporting the use of aspirin for primary prevention of cardiovascular events in high-risk patients (1). The authors used data from 5 RCTs to construct a model of the estimated benefits and harms of aspirin for patients at different 5-year risks for CAD events. In patients with a 5-year risk ≤ 1%, the harm of therapy outweighed the benefits; for those with a 5-year risk ≥ 3%, the benefits exceeded the harm. Neither mortality nor stroke was reduced. Patients benefited from a reduction in MI, which was balanced by increases in GI bleeding and hemorrhagic stroke. The studies reviewed had limited power to detect increases in hemorrhagic stroke.

It makes sense that patients at higher risk are more likely to benefit from aspirin therapy, as has been shown for secondary cardiovascular disease prevention (2). However, we share the authors' concerns about extrapolating data from the population studied to high-risk groups. For example, in the TPT, older patients did not benefit from aspirin, whereas younger patients did; aspirin benefited those with systolic blood pressure (SBP) < 130 mm Hg but not those with SBP > 145 mm Hg. In the PHS, aspirin benefited those with lower cholesterol levels more than those with higher levels (3). However, these are subgroup analyses and may not be valid. Furthermore, we do not know if we can extrapolate these results to women.

The new USPSTF recommendation on aspirin for primary prevention should be placed in the context of primary prevention of cardiovascular disease through smoking cessation, dietary modification, and treatment of hypertension and hyperlipidemia. These measures may be more important because they are well proved, do not increase risk for bleeding, and are associated with lower numbers needed to treat (2).

Meera Jain, MD
Mark Rosenberg, MD
Providence Portland Medical Center
Portland, Oregon, USA

References

1. **U.S. Preventive Services Task Force.** Ann Intern Med. 2002;136:157-60.
2. **Antiplatelet Trialists' Collaboration.** BMJ. 1994;308:81-106.
3. **Steering Committee of the Physicians' Health Study Research Group.** N Engl J Med. 1989;321:129-35.