Review: Antiplatelet therapy prevents occlusive vascular events in high-risk patients

Antithrombotic Trialists' Collaboration. **Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients.** BMJ. 2002 Jan 12;324:71-86.

QUESTION

In patients at high risk for occlusive vascular events because of preexisting disease, how effective is antiplatelet therapy?

DATA SOURCES

Studies were identified by searching 5 databases and trial registers of the Cochrane Stroke and Peripheral Vascular Disease groups; hand searching journals, abstracts, and meeting proceedings; scanning reference lists of trials and review articles; and contacting pharmaceutical companies and experts.

STUDY SELECTION

Randomized controlled trials were selected if they were available by September 1997 and compared an antiplatelet regimen with a control regimen or with another antiplatelet regimen in patients at high risk (> 3%/y) for vascular events because of a previous occlusive event or predisposing condition. Included trials had to have adequate allocation concealment and be unconfounded.

DATA EXTRACTION

Trial coordinators were contacted to obtain details about randomization, allocation concealment, duration of treatment, and follow-up. The primary outcome was a serious vascular event (nonfatal myocardial infarction, nonfatal stroke, or death from a vascular or unknown cause).

MAIN RESULTS

287 trials were included. 197 trials compared antiplatelet therapy with control therapy (195 trials provided vascular event data), and 90 trials compared different antiplatelet regimens (89 trials provided vascular event data). For all high-risk patients, antiplatelet therapy led to lower rates of serious vascular events than control therapy ($P < 0.001$) (Table). The rates were also lower for each of 5 high-risk categories ($P < 0.001$) (Table) as well as for "other" high-risk conditions, including peripheral arterial disease (proportional reduction 23%, 95% CI 15% to 31%). An increased risk for major extracranial bleeding occurred with antiplatelet therapy (odds ratio 1.6, CI 1.4 to 1.8). Among trials comparing different antiplatelet regimens, aspirin was better than no aspirin, and daily doses of 75 to 150 mg were at least as effective as higher doses.

CONCLUSION

In patients at high risk for occlusive vascular events because of preexisting disease, antiplatelet therapy reduces the risk for nonfatal myocardial infarction, nonfatal stroke, or death from vascular or unknown causes.

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Antiplatelet vs control therapy for serious vascular events (mean 0.7 to 29 mo of treatment)*

High-risk category	Number of trials	Adjusted event rates		RRR (95% CI)	NNT (CI)
		Antiplatelet	Control		
All trials	195	10.7%	13.2%	19% (16 to 21)	41 (36 to 48)
Previous MI	12	13.5%	17.0%	21% (16 to 26)	28 (22 to 39)
Acute MI	15	10.4%	14.2%	27% (21 to 32)	26 (21 to 35)
Previous stroke or TIA	21	17.8%	21.4%	17% (12 to 21)	28 (22 to 39)
Acute stroke	7	8.2%	9.1%	10% (4.3 to 16)	108 (68 to 261)
Other high-risk condition	140	8.0%	10.2%	21% (16 to 26)	46 (36 to 61)

*Serious vascular events were nonfatal MI, nonfatal stroke, or death from a vascular or unknown cause. MI = myocardial infarction; TIA = transient ischemic attack. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The Antithrombotic Trialists' Collaboration published its first large review in 1994 (1). In this 2002 update, all studies available by September 1997 have been added. Some of the current results merely strengthen those in the 1994 meta-analysis. The long-standing dispute between American and European strokologists about the relative effectiveness of high-dose and low-dose aspirin (2) has finally been resolved: 75 to 150 mg daily is as effective as higher doses in all high-risk patient groups.

Much of the new information concerns high-risk patient groups that had previously been insufficiently studied. We now know that antiplatelet agents also protect against cardiovascular events in patients with stable angina, intermittent claudication, and atrial fibrillation. Previous documentation concerned improved survival in acute MI. Now, it is also well established that antiplatelet drugs have beneficial effects in patients who have unstable angina, undergo coronary angioplasty, or have an acute ischemic stroke.

This meta-analysis clarifies some issues about the benefits and harms of different antiplatelet agents with different mechanisms of action (aspirin, dipyridamole, clopidogrel, and glycoprotein IIb/IIIa inhibitors). In direct comparisons, although sometimes statistically significant, the differences are small in absolute numbers. For instance, the number needed to treat is about 200 per year to prevent 1 cardiovascular event when clopidogrel is compared with aspirin (at a cost that is about 60 times higher). The authors conclude that aspirin, 75 to 150 mg daily, remains the first choice in the long-term prevention of cardiovascular events. The net benefits of a combination of 2 different antiplatelet agents are best documented in acute cardiac conditions with exceptionally high risk, such as unstable angina and percutaneous coronary interventions (supported by the results of a recently published trial) (3).

Few trials have lasted > 2 years. Nevertheless, the documented effects of antiplatelet agents across a wide range of patient groups suggest that low-dose aspirin should be given routinely to patients at high or intermediate risk for cardiovascular events (above 2% per year). In most healthy people, the annual risk is well below 1%.

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References

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3. **Mehta SR, Yusuf S, Peters RJ, et al.** Lancet. 2001;358:527-33.

