

## Aspirin in secondary prevention

Secondary prevention refers to the use of drugs to prevent cardiovascular and cerebrovascular events - mainly myocardial infarction or stroke - in people who have already experienced such an event or who have a high risk of an event because they have symptomatic coronary heart disease (e.g. angina) or have undergone coronary surgery (e.g. angioplasty).

Aspirin is one of several drugs recommended as secondary prevention (others include beta-blockers, ACE inhibitors and statins); these are used in conjunction with measures such as lifestyle change and stopping smoking to reduce an individual's overall risk of further cardiovascular events. All current guidelines on reducing the risk of cardiovascular events recommend low-dose aspirin for secondary prevention, including those of the National Institute for Health and Clinical Excellence in the UK ([www.nice.org.uk](http://www.nice.org.uk)), the American College of Cardiology ([www.acc.org](http://www.acc.org)) and the European Society of Cardiology ([www.escardio.org](http://www.escardio.org)).

### *Benefits of aspirin as secondary prevention*

The use of aspirin as secondary prevention is supported by strong evidence from two systematic reviews. The first included 195 randomised controlled trials of antiplatelet drugs (predominantly aspirin) in 135,640 high-risk patients (1). Overall, the incidence of new serious events (heart attack, stroke or related death) in patients taking placebo was 13.2% compared with 10.7% in those taking an antiplatelet drug. This represents a reduction of 22% in the odds of a serious vascular event in people taking an antiplatelet drug and was highly statistically significant ( $p < 0.0001$ ). For aspirin alone, a dose of 75 - 150 mg/day was associated with an odds reduction of vascular events of 32%.

- In patients who had previously had a myocardial infarction the review found that, for every 1,000 patients taking antiplatelet therapy for just over 2 years, there would be 18 fewer non-fatal myocardial infarctions, 5 fewer non-fatal strokes and 14 fewer deaths due to vascular events.
- In patients with a history of stroke or transient ischaemic attack ('mini-stroke') taking antiplatelet therapy for 29 months, treatment would result in 36 fewer serious vascular events, largely due to a reduction in non-fatal stroke (25 fewer per 1,000) but including 6 fewer non-fatal myocardial infarctions per 1,000 patients. Death from any cause would also be reduced by 15 per 1,000.
- The risk of serious vascular events was reduced by:
  - 46% in patients with unstable angina
  - 33% in patients with stable angina
  - 23% in patients with peripheral arterial disease
  - 53% in patients undergoing coronary angioplasty.

This review also found that doses of 75 - 150 mg/day and higher doses of aspirin were equally effective.

The second study was a meta-analysis of 6 trials involving 6,300 patients randomised to placebo or low-dose aspirin (up to 325 mg/day) for secondary prevention (2). This study differed from the first in excluding other antiplatelet drugs and restricting the patients studied to those eligible to take aspirin to prevent myocardial infarction or stroke.

Aspirin was associated with a 30% reduction in both vascular deaths ( $p < 0.001$ ) and myocardial infarction ( $p < 0.001$ ) compared with placebo and an 18% reduction in the risk of all-cause death ( $p = 0.03$ ). It was also associated with a 20% lower risk of stroke but this difference was not statistically significant ( $p = 0.07$ ).

#### *Complications of aspirin as secondary prevention*

Systematic reviews that have specifically addressed the risk of complications with aspirin (3) have shown that:

- the risk of any bleeding complication with aspirin at a dose less than 100 mg/day is 3.6% but higher doses are associated with greater risk
- the risk of intracranial bleeding is estimated at 0.1 - 0.3% for doses below 325 mg/day
- the risk of serious extracranial bleeding causing death or requiring transfusion was increased by a factor of 1.6, equivalent to an additional one case per 1,000 patients with previous myocardial infarction (2)
- the risk of gastrointestinal bleeding is increased by a factor of 1.68 - 2.5; the risk is lower at doses of less than 100 mg/day (1.1%) than 100 - 325 mg/day (2.4%)

#### *Combining aspirin with other drugs*

Most patients who take low-dose aspirin for secondary prevention do not take other antiplatelet drugs. However, aspirin may occasionally be combined with clopidogrel or dipyridamole in specific groups of patients (e.g. patients with acute coronary syndrome or stroke respectively).

#### *Summary*

In patients who have already experienced cardiovascular events or are at high risk, aspirin substantially reduces the risk of death and further cardiovascular events. The large reductions in risk far outweigh the risks associated with adverse effects.

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

2. Weisman SM, Graham DY. Evaluation of the benefits and risks of low-dose aspirin in the secondary prevention of cardiovascular and cerebrovascular events. *Arch Intern Med* 2002;162:2197–2202

3. Gami A. Secondary prevention of ischaemic cardiac events. Aspirin. In: *Clinical Evidence*. BMJ Publishing Group. 1st December 2005 ([www.clinicalevidence.com/ceweb/conditions/cvd/0206/0206\\_I21.jsp](http://www.clinicalevidence.com/ceweb/conditions/cvd/0206/0206_I21.jsp); accessed 3.7.06)

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