Aspirin and vascular disease – an update

Investigations into the multifactorial nature of cardiovascular disease continue to be reported. It is generally agreed that there are two necessary precipitating events for a coronary – a damaged artery (atherosclerosis) and. as a trigger, a thrombosis. Platelet aggregation has a significant part to play in the formation of thrombi. In 1980, the Lancet concluded from six reports covering over 10,000 patients that aspirin (about 1000 mg/day) significantly reduced cardiovascular mortality and morbidity in patients who had previously suffered a myocardial infarction. Over the past twenty years, aspirin has been found to inhibit platelet function via an effect on prostaglandin synthesis. These discoveries of a potential antithrombotic effect prompted an investigation in 5000 healthy British male doctors of the potential of aspirin to prevent both cerebrovascular and cardiovascular disease (Peto et al, 1988). A daily dose of 500mg of aspirin over a six year period did not produce a statistically significant result but the authors conclude that the confidence intervals of the study do not exclude a beneficial effect of aspirin of about 10–20%. Such a result is perhaps not unexpected since vascular events in healthy people are not common and so very large study populations are needed for a reliable determination of an effect on incidence.

A second study, involving approximately four times as many American doctors was also initiated and preliminary results have just been reported. This American study had two main aims. Firstly, to find out whether 325mg aspirin taken on alternate days reduces mortality from cardiovascular disease and secondly to assess whether 50mg beta-carotene on alternate days decreases the incidence of cancer. The aspirin part of the study was completed ahead of schedule because of the surprisingly large and highly significant reduction in the incidence of non-fatal and fatal myocardial infarction. Overall there was a 47% reduction in the risk of total myocardial infarction, but for strokes there was a non-significant 15% increase among those receiving aspirin. The risk appeared greater with respect to haemorrhagic strokes. Clearly before any conclusions can be reached, further analysis of this second trial is needed since half the doctors receiving aspirin also received betacarotene. However, this larger study suggests that aspirin may have a role to play in the prevention of cardiovascular disease. Taken together, the two studies suggest that prophylactic antiplatelet treatment may avert about one third of non-fatal myocardial infarctions. However, currently, neither study suggests any reduction in overall mortality.

Two other reports published recently give additional information on the effect of aspirin in the secondary prevention of vascular disease. Patients who have had a mild ischaemic attack are at risk of a recurrence, which could be permanently disabling or fatal. Because of its reported effect on thrombosis prevention, aspirin may have a role to play in reducing this risk. In the United Kingdom Transient Ischaemic Attacks Aspirin trial (UK-TIA, 1988), 2400 patients received a placebo, 300mg aspirin once daily or 600mg aspirin twice daily over a four year period following a transient ischaemic attack. Although the chance of suffering a non-fatal myocardial infarction, a non-fatal major stroke, vascular death or non-vascular death was reduced significantly by 18% in the patients receiving aspirin, this was partly due to an unexpected fall in non-vascular deaths. Consequently the trial yielded no conclusive results.

Another recent review covers 25 randomised trials, including 29,000 patients (Antiplatelet Trialists Collaboration, 1988). Antiplatelet drugs were used for secondary prevention in patients with a history of transient ischaemic heart attacks, occlusive stroke, unstable angina or myocardial infarction. Drug treatment had no effect on non-vascular mortality but significantly reduced vascular mortality by 15% and non-fatal strokes and myocardial infarction by 30%. Aspirin is reported to be at least as good as any other drug as an antiplatelet agent and doses of 300mg/day were just as effective as larger doses. In the authors' view, these studies indicate that antiplatelet treatment can reduce the incidence of serious vascular events by about a quarter among a wide range of patients at particular risk of occlusive vascular disease. It is as yet unclear whether these effects apply equally to men and women. This is partly due to the fact that men significantly outnumbered women in the trials.

In conclusion, there is evidence that regular aspirin may be of value for people who have previously suffered cardiovascular or cerebrovascular problems. However, various questions still need to be answered including whether aspirin has a role in primary prevention in healthy people and whether aspirin could exacerbate haemorrhagic stroke as opposed to occlusive stroke, due to its apparent anti-thrombotic properties. Because of the known gastro-toxic effect of large doses of aspirin, it is recommended that any aspirin used should be in the enteric-coated form.

References:

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