Aspirin but not vitamin E prevented cardiovascular events in patients at risk

Collaborative Group of the Primary Prevention Project (PPP). ***Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice.*** *Lancet 2001 Jan 13;**357**:89–95.*

QUESTION: In patients with ⩾1 cardiovascular risk factor but no history of cardiovascular disease, do aspirin and vitamin E prevent cardiovascular events?

Design

Randomised (allocation concealed), unblinded, 2 × 2 factorial trial with a mean follow up of 3.6 years.

Setting

315 general practices and 15 hospital hypertension units in Italy.

Patients

4495 patients (mean age 64 y, 58% women) aged ⩾50 years who had ⩾1 major cardiovascular risk factor: age ⩾65 years, hypertension, hypercholesterolaemia, diabetes mellitus, obesity, and family history of myocardial infarction (MI) before 55 years of age in ⩾1 parent or sibling. Exclusion criteria were treatment with antiplatelet drugs, chronic use of anti-inflammatory agents or anticoagulants, contraindication to aspirin, disease with a poor short term prognosis, or psychological or logistic problems known to affect compliance. Follow up was 92%.

Intervention

Patients were allocated to aspirin, one 100 mg enteric coated tablet per day (n = 2226) or no aspirin (n = 2269) and to vitamin E, one 300 mg (300 IU) synthetic α tocopherol capsule (n = 2231) or no vitamin E (n = 2264).

Main outcome measures

The primary outcome was a combined endpoint of cardiovascular death, non-fatal MI, and non-fatal stroke. Secondary outcomes were cardiovascular deaths, total deaths, and total cardiovascular events.

Main results

Analysis was by intention to treat. The trial was stopped early because evidence from 2 large trials indicated a benefit of aspirin in cardiovascular primary prevention that was borne out by the planned interim analysis in this trial. Patients who received aspirin had a significantly reduced risk for cardiovascular death (p = 0.049) and total cardiovascular events (p = 0.014), but the groups did not differ statistically for the main combined endpoint or for any other outcome (table). Patients who received vitamin E had no reduction in risk for any outcomes except for the incidence of peripheral artery disease (0.7% *v* 1.3%, p = 0.043).

Conclusion

In patients with cardiovascular risk but no history of cardiovascular disease, aspirin but not vitamin E prevented cardiovascular events.

COMMENTARY

Several factors may contribute to the prevention of cardiovascular disease. The Primary Prevention Project (PPP) focuses on low dose aspirin and vitamin E. In a recent review of 4 randomised trials of aspirin for the primary prevention of vascular disease,[1] 3 of the 4 studies reviewed did not include women. An important aspect of the PPP study is the inclusion of women (58%) and therefore the enhanced ability to generalise the benefits of aspirin treatment to women. The findings suggest that the use of low dose aspirin may be an effective means of reducing cardiovascular events in women who are at risk. The PPP does not provide evidence that vitamin E reduces cardiovascular risk. However, because of the early termination of the trial, the PPP was not adequately powered to test the vitamin E hypothesis.

The results of the PPP study are important to nurses who work in cardiovascular nursing, public health, and women's health. The results support the use of low dose aspirin in the care of men and women at risk for cardiovascular disease. Additional trials are needed to determine the effect of low dose aspirin on stroke and bleeding complications. Furthermore, additional trials with women are needed to better understand the effect of accepted treatments commonly used in men. The Women's Health Initiative, investigating aspirin treatment among 40 000 women, will provide more evidence of the benefits and risks of aspirin in healthy women.

At present, the decision to recommend aspirin needs to be made in conjunction with an assessment of an individual's cardiovascular risk factors, weighed against their personal risk of bleeding and stroke. Aspirin should be considered an adjunct to other primary prevention strategies.

Heather Sherrard, RN, MHA, CHE
Vice President, Clinical Services
University of Ottawa Heart Institute
Ottawa, Ontario, Canada

1 Hebert PR, Hennekens CH. An overview of the 4 randomized trials of aspirin therapy in the primary prevention of vascular disease. *Arch Intern Med* 2000;**160**:3123–7.

*Aspirin v no aspirin and vitamin E v no vitamin E for patients with major cardiovascular risk factors**

Outcomes at mean of 3.6 years	Comparison	Event rates	RRR (95% CI)	NNT (CI)
Combined endpoint	Aspirin *v* no aspirin	2.0% *v* 2.8%	29% (–4 to 52)	Not significant
Cardiovascular death	Aspirin *v* no aspirin	0.8% *v* 1.4%	44% (1 to 69)	166 (81 to 62500)
Total cardiovascular events	Aspirin *v* no aspirin	6.3% *v* 8.2%	23% (5 to 38)	53 (30 to 258)
			RRI (CI)	NNH
Combined endpoint	Vitamin E *v* no vitamin E	2.5% *v* 2.3%	7% (–56 to 26)	Not significant

*Combined endpoint = cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke. Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

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For correspondence: Dr M C Roncaglioni, Istituto di Ricerche Farmacologiche "Mario Negri," Via Eritrea 62, 20157 Milan, Italy. Fax +39 02 39001916.

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Notes