

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, how effective is treatment with aspirin and vitamin E in preventing cardiovascular events?

DESIGN

Randomized (allocation concealed*), unblinded,* 2×2 factorial trial with mean 3.6-year follow-up.

SETTING

315 general practices and 15 hospital hypertension units in Italy.

PATIENTS

4495 patients who were ≥ 50 years of age (mean age 64 y, 58% women) and had ≥ 1 major cardiovascular risk factor: age ≥ 65 years, hypertension, hypercholesterolemia, 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 to no aspirin ($n = 2269$), and to vitamin E,

one 300-mg (300 IU) synthetic α -tocopherol capsule ($n = 2231$), or to no vitamin E ($n = 2264$).

MAIN OUTCOME MEASURES

The primary outcome was a combined end point of cardiovascular death, nonfatal MI, and nonfatal 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 no statistically signif-

icant difference existed between groups for the main combined end point or for any other outcome (Table). Patients who received vitamin E did not show reduced risk for any outcomes except for the incidence of peripheral artery disease (0.7% vs 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.

Sources of funding: Medical Department of Bayer Italy; aspirin preparation supplied by Bayer; vitamin E capsules supplied by Bracco SpA.

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

*See Glossary.

Aspirin vs no aspirin and vitamin E vs no vitamin E for patients with major cardiovascular risk factors†

Outcomes at mean of 3.6 y	Comparison	Event rates	RRR (95% CI)	NNT (CI)
Combined end point	Aspirin vs no aspirin	2.0% vs 2.8%	29% (-4 to 52)	Not significant
Cardiovascular death	Aspirin vs no aspirin	0.8% vs 1.4%	44% (1 to 69)	166 (81 to 62 500)
			RRI (CI)	NNH
Combined end point	Vitamin E vs no vitamin E	2.5% vs 2.3%	7% (-56 to 26)	Not significant

†Combined end point = cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

The Primary Prevention Project (PPP) trial substantially strengthens the existing evidence supporting the use of aspirin to prevent cardiovascular events. The most important feature of this trial is its study design. In contrast to previous prevention trials with aspirin, the PPP trial enrolled a broad-based patient population. The inclusion criteria were liberal; patients were enrolled from community-based practices, and $> 50\%$ of the enrolled patients were women. Previous prevention trials enrolled men or higher-risk patients. Patients were eligible for the PPP trial simply by being ≥ 65 years of age or obese (body mass index > 30 kg/m²).

As in other recently published clinical trials (1), vitamin E failed to provide any benefit in preventing cardiovascular events. The potential benefit of vitamin E is either very small or requires a longer period of ingestion than can be practically shown with a clinical trial.

In summary, low doses (80 to 100 mg) of enteric-coated aspirin substantially lower the risk for cardiovascular events. In the absence of uncontrolled hypertension or other contraindications, practicing physicians should recommend aspirin for their patients who are ≥ 65 years of age or those with other known cardiovascular risk factors. The addition of vitamin E cannot be firmly recommended on the basis of the available evidence.

Robert Gluckman, MD
Providence–St. Vincent Medical Center
Portland, Oregon, USA

Reference

1. Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med*. 2000;342:154-60.