

Diabetic vascular disease and aspirin: no effect in primary prevention

Background

Several large trials of aspirin for primary prevention have examined its effects in subgroups of patients with diabetes; however, these subgroup analyses have not demonstrated a significant effect on the reduction of vascular events.¹ The American Diabetes Association recommends the use of aspirin (75–162 mg/day) as a primary prevention strategy in patients with diabetes who are at increased risk for cardiovascular (CV) disease, including those who are older than 40 years or who have additional risk factors, such as family history of coronary heart disease, hypertension, smoking, dyslipidemia, or albuminuria,² despite the fact that the evidence for an effect of aspirin in primary prevention is weak. In contrast, in the European (European Society of Cardiology and European Association for the Study of Diabetes) guidelines, there is no mention of aspirin for the primary prevention of myocardial infarction or CV death, while it is recommended for the prevention of stroke.³

Aspirin in primary prevention

Very recently, two primary prevention trials with aspirin in diabetic patients were reported from Japan⁴ and Scotland.⁵

In the **Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD)** trial, 2539 patients with type 2 diabetes and no history of atherosclerotic disease were included.⁴ The patients received either aspirin (81 or 100 mg per day) or placebo for 4.4 years. There was a nonsignificant trend toward fewer atherosclerotic events in the aspirin versus non-aspirin group (13.6 vs 17.0 per 1000 person-years) (HR, 0.80; 95% CI, 0.58–1.10; P=0.16). The combined end point of fatal coronary events and fatal cerebrovascular events occurred in 1 patient (stroke) in the aspirin group and 10 patients (5 fatal myocardial infarctions and 5 fatal strokes) in the non-aspirin group (HR, 0.10; 95% CI, 0.01–0.79; P=0.004). A total of 34 patients in the aspirin group and 38 patients in the non-aspirin group died from any cause (HR, 0.90; 95% CI, 0.57–1.14; P=NS). The composite of hemorrhagic stroke and significant gastrointestinal bleeding was not significantly different between the aspirin and non-aspirin groups. The authors concluded that low-dose aspirin as primary prevention did not reduce the risk of cardiovascular events in Japanese type 2 diabetic patients.

The **Prevention Of Progression of Asymptomatic Diabetic Arterial Disease (POPADAD)** study included 1276 adults aged 40 or more with type 2 diabetes and an ankle brachial pressure index of 0.99 or less but no symptomatic CV disease.⁵ In the antiplatelet arm of the study, the patients received either aspirin (100 mg per day) or placebo for 6.7 years. The observed risk of a major CV event was 2.9% a year. There was no difference in the primary CV disease events between the aspirin and non-aspirin group (18.2% v 18.3%; HR 0.98). A subgroup analysis in those with an index of 0.91–0.99 or less also did not show any benefit of aspirin. In addition, 43 deaths from coronary heart disease or stroke occurred in the aspirin groups, compared with 35 in the non-aspirin groups (6.7% v 5.5%; HR 1.23).

Aspirin in secondary primary prevention after myocardial infarction

In a cohort study involving 2499 patients with acute coronary syndrome recruited from 11 UK hospitals, multivariable analysis was performed comparing all-cause mortality risk reduction associated with pharmacologic agents in patients with and without diabetes.⁶ Aspirin was not associated with significant mortality benefit in diabetes sufferers, whereas nondiabetic patients derived a 48% mortality reduction (P<0.001). The authors concluded that aspirin is associated with less effective mortality reduction in patients with diabetes and unstable coronary artery disease, whereas comparable benefit for diabetic and nondiabetic patients was noted for other secondary prevention agents such as statins, β -blockers, and angiotensin converting enzyme (ACE) inhibitors.

In conclusion, a total of seven well-controlled trials now show that aspirin has no benefit for primary prevention of cardiovascular events, even in people at higher risk.⁷ Although aspirin is cheap and universally available, practitioners and authors of guidelines need to heed the evidence that aspirin should be prescribed only in patients with established symptomatic CV disease.

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