COMMENTS AND RESPONSES

Primary Prevention of Cardiovascular Diseases in People With Diabetes Mellitus: A Scientific Statement From the American Heart Association and the American Diabetes Association

Response to Buse et al.

The recent American Diabetes Association/American Heart Association statement recommends the use of low doses of aspirin as a strategy for primary prevention of cardiovascular diseases in all individuals with diabetes aged >40 years or who have additional risk factors (1). Like in previous recommendations (2), only selected pieces of evidence are mentioned to support this statement. The data used to sustain the efficacy of aspirin come from the Early Treatment Diabetic Retinopathy Study, the only study specifically conducted in diabetic patients with and without previous cardiovascular disease (3). In this trial, treatment with 650 mg aspirin for 5 years was associated with a nonsignificant 9% reduction in the primary end point (vascular death, nonfatal myocardial infarction, or nonfatal stroke). On the other hand, the results of the last meta-analysis on the efficacy of antiplatelet therapy in the prevention of major cardiovascular events are not discussed (4). The meta-analysis documented a clear benefit for the whole population (22% reduction in the risk of major cardiovascular events) but not for the subgroup of diabetic patients (7% risk reduction). Likewise, the Primary Prevention Project, involving over 1,000 diabetic patients, showed that low-dose aspirin only marginally reduced the risk of major cardiovascular events (RR 0.90 [95% CI 0.50–1.62]) (5). More recently, results of the Women's Health Study documented in 1,027 women with diabetes that treatment with low-dose aspirin was associated with a nonsignificant 10% reduction in the risk of major cardiovascular events as compared with placebo (0.90 [0.63–1.29]). The overall effect was the result of a reduction in the risk of stroke (0.46 [0.25–0.85]), associated with an increased risk of myocardial infarction (1.48 [0.88–2.49]) (6).

Overall, existing data suggest that the clinical efficacy of low-dose aspirin in patients with diabetes is substantially lower than in individuals without diabetes. Indeed, a growing body of evidence supports the hypothesis that diabetes might represent a special case of aspirin resistance (7). Therefore, existing recommendations seem mainly based on extrapolations from data on other high-risk groups, rather than a comprehensive review of pertinent data, under the assumption that diabetes is a cardiovascular disease risk equivalent.

The need for sound, reliable evidence is underlined by the activation of several large-scale randomized trials (ASCEND [A Study of Cardiovascular Events in Diabetes], POPADAD [Prevention of Progression of Asymptomatic Diabetic Arterial Disease], ACCEPT-D [Aspirin and Simvastatin Combination for Cardiovascular Events Prevention Trial in Diabetes], and J-PAD [Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes]) currently under way. In the meantime, the decision to prescribe aspirin should be taken on an individual patient basis, after a careful evaluation of the balance between the expected benefits and the risk of major bleeding (8). Will aspirin benefits outweigh the risks in patients younger than 50 years of age, without additional cardiovascular risk factors? Should aspirin be prescribed to patients over 70 years of age, considering the lack of reliable information in this age-group and the sharp increase in the risk of upper gastrointestinal bleeding? (9). If the lower-than-expected benefit of aspirin in diabetes will be confirmed by ongoing trials, its use for primary prevention of vascular disease in unselected people will result in net harm. To this respect, it is worth noting that the Food and Drug Administration did not support using aspirin for the primary prevention of heart attacks in moderate-risk patients.

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