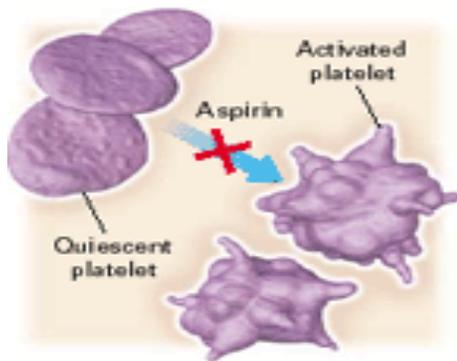


ASPIRIN UPDATE

Number 69

June 2002



This *Heartbeat* will cover the new recommendations from the US task force on use of aspirin (ASA) for primary prevention of coronary heart disease (CHD). Evidence supporting various strategies, when they exist, will be presented along with recommendations of what the optimum dose of ASA should be for both primary and secondary prevention.

The Clinical Problem

The primary prevention of CHD involves the deliberate treatment of high-risk patients in order to prevent coronary events in those without manifest disease. Approximately 25% of the reduction in the rate of death from CHD that has occurred in the past 30 years may be explained by the practice of primary prevention.

In addition to the established risk factors of hypertension, smoking, hypercholesterolemia, diabetes mellitus and sedentary lifestyle, all of which have been identified as targets for primary prevention, the risk of clinical CHD is related to platelet activity and inflammation. Because ASA has both anti-platelet and anti-inflammatory effects it has been proposed and tested for use in prevention.

Recommendation

In secondary prevention the benefit of decreased events readily outweighs the possible risks (hemorrhage) and the decision to treat is easy. In primary prevention the balance between benefit and risk is not as clear.

The US Preventive Services Task Force (USPSTF) strongly recommends that clinicians discuss ASA prevention with adults who are at increased risk of CHD.¹ Discussion with patients should address both the potential benefits and harms of ASA therapy. The USPSTF found good evidence that ASA decreases the incidence of CHD in adults who are at increased risk for it. But it also found good evidence that ASA increases the risk of GI bleeding and fair evidence that ASA increases the risk of hemorrhagic strokes. The USPSTF guideline concludes that the balance of benefits and harms is “most favorable” in patients at higher risk, that is, a 5-year risk of 3% or higher, “but this is influenced by patient preferences.”

Evidence

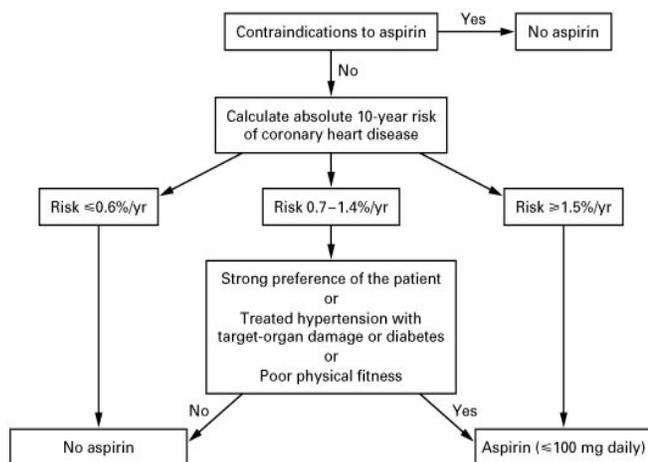
These recommendations were based on a meta-analysis of the 5 major randomized trials of ASA for primary prevention.² When the 5-year absolute risk of coronary events reached 5%, ASA treatment reduced the absolute risk of coronary events by 0.3% per year but increased the risk of hemorrhagic stroke by 0.02% per year and the risk of major GI bleeding by 0.06% per year. In contrast, when the 5-year absolute risk of coronary events was only 1%, ASA treatment resulted in a reduction of only 0.06% per year in the absolute risk.

Strategy: Practical Application

The clinician needs to sit down with the patient and discuss the relative benefits and potential harms of ASA therapy based on their risk of having a coronary event. The absolute risk of having a major coronary event should be calculated from the Framingham risk score (CHD Risk Calculator-on this site), so that people can make informed decisions regarding the use of ASA. This scoring system obviously isn't perfect (doesn't take family history into account because of unreliability of history) but is significantly better than just counting risk factors.

A suggested algorithm (Fig. 1) for making decisions about ASA therapy on the basis of predictions of absolute risk of coronary events is presented below.³

Figure 1. Suggested Algorithm for Making Decisions about the Use of ASA for Primary Prevention of CHD.



Contraindications to ASA therapy include allergy, bleeding diathesis, platelet disorders, and active peptic ulcer disease. Relative contraindications include renal failure, concurrent use of nonsteroidal anti-inflammatory agents or anticoagulants and uncontrolled hypertension. The risk of CHD is estimated with the use of the Framingham risk score. Poor physical fitness is defined as impaired exercise capacity for age and sex.

Patients with an absolute risk of 1.5% per year (15% per 10 years) or higher are, barring contraindications, good candidates for ASA

therapy. Patients with an absolute risk of 0.6% per year (6% per 10 years) or less are probably not good candidates. In patients with an intermediate risk—that is, 0.7% to 1.4% per year—other factors should be considered such as patient preferences, family history or poor physical fitness (inability to complete 3 minutes of Stage 1 Bruce protocol stress test [5 METS]). Treatment should seriously be considered for those with controlled hypertension and target organ damage. Most would recommend treating all diabetics over age 30 (unless contraindicated) since they are now considered to have CHD equivalent disease.

Optimum Dosage?

There have been no primary or secondary prevention studies comparing different doses of ASA. It is also unclear whether the risk of major bleeding is associated with the dose of ASA. In the 5 primary prevention studies, the doses of ASA varied from 75 mg to 650 mg once a day.

When asked recently, however, experts were in agreement that lower doses of ASA seemed equally effective in preventing CHD events than higher doses and would probably result in less gastric side effects.⁴ All said they would recommend doses of 75 or 81mg for chronic use in heart patients, but higher doses were preferable for acute situations (the initial 4 weeks after an acute event or intervention). The strength of the low dose ASA varies between the US and the UK. The doses came from splitting conventional ASA tablets into quarters (325 to 81 mg in the US and 300 to 75 mg in the UK).

Dr Richard Peto (Radcliffe Infirmary, Oxford, UK) one of the authors of a recent anti-platelet meta-analysis⁵ commented, “There is no good evidence that higher doses are any better than 75 mg for long-term use.” The full anti-platelet effect is seen at these lower doses.

Dr Shamir Mehta (McMaster University, Hamilton, ON), of the Clopidogrel in Unstable

Angina to Prevent recurrent events (CURE) trial of ASA plus clopidogrel, gave a similar view. “In CURE we saw an increase in major bleeding with increasing doses of ASA, but there did not seem to be any difference in efficacy with different doses.”

Dr Eric Toprol (Cleveland Clinic Foundation) has broadly the same view as the other experts. “The data makes a cogent case for dropping the dose of ASA to 81-162 mg. It would be nice to have data from a dedicated mega-trial, but until that time we should be avoiding 325 mg as it appears to carry more bleeding liability.”

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Heartbeats can be found at www.sjhg.salu.net under Patient Education, then From Your Physician.

¹ US Preventive Services Task Force. Aspirin for the primary prevention of cardiovascular events: recommendations and rationae. *Ann Intern Med* 2002; 136: 157-60.

² Hayden M, et al. Aspirin for primary prevention of cardiovascular events: A summary of the evidence for the US Preventive Services Task Force. *Ann Intern Med* 2002; 136: 161-72.

³ Lauer M. Aspirin for primary prevention of coronary events. *N Engl J Med* 2002; 346: 1468-74.

⁴ www.theheart.org

⁵ Collaborative meta-analysis of randomized trials of anti-platelet therapy for prevention of death, myocardial infarction, and stroke in high-risk patients. *BMJ* 2002; 324: 71-86.