Benefits and Harms of Warfarin plus Aspirin after Acute Coronary Events

Summaries for Patients are a service provided by *Annals* to help patients better understand the complicated and often mystifying language of modern medicine.

The full report is titled "Warfarin plus Aspirin after Myocardial Infarction or the Acute Coronary Syndrome: Meta-Analysis with Estimates of Risk and Benefit." It is in the 16 August 2005 issue of *Annals of Internal Medicine* (volume 143, pages 241-250). The authors are M.B. Rothberg, C. Celestin, L.D. Fiore, E. Lawler, and J.R. Cook.

What is the problem and what is known about it so far?

Clogged heart arteries can cause acute coronary events, such as heart attacks or worsening chest pain (unstable angina). Many middle-aged and older adults have these life-threatening events. They are a major cause of medical care and hospitalization in developed countries. Adults who survive the events often have high risks for blood clots in the heart's arteries and for repeated events. Doctors usually prescribe aspirin to help prevent further clots and repeated events. They may also prescribe a "blood thinner" (warfarin) or both aspirin and warfarin. Warfarin requires frequent monitoring and sometimes causes problems with bleeding. Doctors sometimes wonder if giving both aspirin and warfarin leads to more harms than benefits.

Why did the researchers do this particular study?

To summarize literature about the benefits and harms of warfarin plus aspirin for people who have had an acute coronary event.

Who was studied?

5938 adults included in 10 randomized trials. All had either a heart attack or unstable angina. None received stent procedures to open up blocked blood vessels.

How was the study done?

The authors looked for studies published between 1990 and October 2004. They selected randomized trials that compared regular-intensity warfarin (international normalized ratio > 2.0) plus aspirin with aspirin alone in patients with acute coronary events. They combined data from these studies to estimate chances of benefits (reductions in heart attacks, ischemic strokes, and heart artery procedures) and harms (major bleeding events). They then applied numbers from the combined benefit and harm data (rate ratios) to a large population-based study that included many patients with different risks for heart events and bleeding. The researchers estimated groups of people for whom warfarin plus aspirin might be more helpful than harmful.

What did the researchers find?

Compared with aspirin alone, warfarin plus aspirin decreased annual rates of heart attacks, ischemic strokes, and heart artery procedures. Warfarin plus aspirin increased annual rates of major bleeding. Patients with several risk factors, such as older age, diabetes, heart failure, and decreased kidney function, had the highest risks for heart attacks and strokes. Older patients who previously had a stroke, gastrointestinal bleeding episode, kidney disease, or atrial fibrillation were at higher risk for bleeding. Numbers of deaths did not differ between treatments. In patients with low or average risk for bleeding, the numbers of heart and stroke events prevented with combination therapy exceeded the numbers of major bleeding episodes that it caused.

What were the limitations of the study?

Doctors treat many patients with acute coronary events with stents. They don't use warfarin in these patients because of bleeding risks associated with the stent procedure. This review's findings do not apply to patients treated with stents. Also, the researchers sometimes used assumptions when they applied data to different patient groups.

What are the implications of the study?

Benefits of warfarin plus aspirin may outweigh harms for some patients with acute coronary events who are not stented and do not have high bleeding risks.