

Medscape Conference Coverage, based on selected sessions at the:

[European Society of Cardiology \(ESC\) Congress 2009](#)

This coverage is not sanctioned by, nor a part of, the [European Society of Cardiology](#).

From [Heartwire](#)



Experts Question Routine Aspirin for Patients With Type 2 Diabetes

Fran Lowry

September 10, 2009 (**Barcelona, Spain**) — The widespread recommendation for the routine use of low-dose aspirin in primary prevention of cardiovascular events for all patients with type 2 diabetes should be revisited, experts said at the **European Society of Cardiology 2009 Congress**.

Currently, most of the major scientific bodies, including the American Heart Association (AHA), American College of Cardiology (ACC), European Society of Cardiology (ESC), and the European Association for the Study of Diabetes (EASD), uniformly recommend giving aspirin to these patients. The lone exception is the Canadian Diabetes Association, which says that the decision to prescribe aspirin should be left to the discretion of the individual physician. Yet there is inadequate trial evidence for the efficacy and safety of low-dose aspirin in this setting, Dr Carlo Patrono (Catholic University, Rome, Italy) told meeting attendees.

"If a patient has had a prior event, there is no question that he or she should be on aspirin, regardless of whether the patient is or is not diabetic, because we have plenty of evidence there," Patrono commented to **heartwire**. "But we don't have evidence for the efficacy and safety of low-dose aspirin in diabetics without a prior vascular event or without overt vascular disease. We need direct randomized evidence."

Patrono was echoed by **Dr Harald Darius** (Vivantes Neukoelln Medical Center, Berlin, Germany), who told **heartwire** that recent trial results appear to contradict the general recommendations by the AHA, ACC, ESC, and EASD. "These societies recommend that every diabetic as soon as the diagnosis is made should receive aspirin as part of the initial therapeutic regimen, but they are probably overestimating the risk of diabetes in otherwise-healthy people."

Indeed, aspirin may be harmful for people with diabetes. "Diabetes mellitus is not only a risk factor for the occurrence of a serious vascular event, which is increased by about two-and-a-half fold, it is also a risk factor for major bleeds, which increase by about 50% in association with diabetes. So we should be very careful in seeking adequate evidence for both efficacy and safety of aspirin in this subgroup," Patrono said.

Routine Aspirin Challenged in Japan, Scotland

In separate presentations, both Darius and Patrono cited new evidence from the **Japanese Primary**

Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) trial, which showed no significant effect of aspirin on reducing cardiovascular events [1]. Another trial--the **Prevention of Progression of Arterial Disease and Diabetes** (POPADAD) study--also failed to find evidence of efficacy from aspirin in 1300 subjects with diabetes and a low ankle-brachial index [2].

"The hazard ratio was 0.498 for the primary end point, which was death from coronary heart disease or stroke. My view is that this is a relatively small study, so the negative findings might be due to inadequate statistical power, but it is disappointing that these studies do not provide any direct evidence for efficacy," Patrono said.

There may be specific reasons why aspirin is not as effective in diabetic individuals, Patrono suggested. These include Cox-1 glycation, faster recovery of Cox-1 activity due to accelerated platelet turnover in a fraction of the diabetic population, and enhanced platelet Cox-2 expression that might be associated with accelerated platelet turnover.

Patrono and colleagues are currently studying the second option. "Our hypothesis is that enhanced platelet turnover in at least a fraction of type 2 diabetic patients may allow sufficient recovery of Cox-1 activity during a 24-hour dosing interval, particularly between 12 and 24 hours, to overcome the antiplatelet effect of low-dose aspirin, thereby limiting its clinical efficacy," he explained.

They tested 100 patients with type 2 diabetes on chronic low-dose (100-mg/day) aspirin, synchronizing their aspirin administration at 8 pm and then again the following day at 8 am, when they took an additional blood sample every three hours to cover the 12- to 24-hour dosing interval. After obtaining a total of five blood samples, they then studied the time course of recovery of platelet Cox-1 and Cox-2 activity in these individuals and found that some patients demonstrated a very slow recovery, comparable to healthy, nondiabetic individuals; others showed intermediate recovery, and still other subjects demonstrated a substantial recovery of platelet Cox-1 activity.

"These preliminary findings have important practical implications," Patrono said. "They may suggest alternative pharmacologic strategies to apply to particular subgroups of diabetic patients, including different dosing strategies to maximize the effect of low-dose aspirin in these patients. The same might apply to other drugs, such as clopidogrel."

Dr Marie-Christine Alessi (Université de la Méditerranée Aix-Marseille, Marseille, France), a moderator of the session, told **heartwire** that she thought Patrono's data showing that aspirin resistance might be explained by differences in platelet turnover was "very interesting. Aspirin--at least as we use it now--may not be useful." She suggested that it might be possible to isolate a population who may benefit through phenotyping. "And perhaps if we change the dosing strategy, for example by dividing the dose of aspirin so that we are giving it twice daily, we could be more protective."

Uncertainty Will Remain Until the Evidence Is In

The uncertainty about the role of aspirin for the prevention of cardiovascular events among patients with diabetes will remain until the results of ongoing trials--such as **A Study of Cardiovascular Events in Diabetes** (ASCEND) and **Aspirin and Simvastatin Combination for CV Events Prevention Trial in Diabetes** (ACCEPT-D)--are in, but this will take at least five years, Darius said.

Meanwhile, the clinical strategy should include aspirin for primary prevention in all diabetics 65 years and older or below 65 years in the presence of at least one additional cardiovascular risk factor such as obesity, hypertension, or dyslipidemia. Patients known to have vascular disease should continue to be offered primary prevention with aspirin, Darius said.

Authors and Disclosures

Journalist

Fran Lowry

is a freelance writer for Medscape.

Heartwire © 2009 Medscape, LLC
