Oral Anticoagulation Therapy During and After Coronary Angioplasty

To the Editor:

We read with great interest the recent article by ten Berg et al. on oral anticoagulant therapy during and after coronary angioplasty. In previous trials on late restenosis after percutaneous transluminal coronary angioplasty (PTCA), oral anticoagulants were not more effective than aspirin as adjunctive treatment after PTCA. However, in those trials, anticoagulant therapy was only started after PTCA. The study by ten Berg et al. revealed that coumarin therapy started before PTCA decreased the incidence of late thrombotic events and improved 6-month angiographic outcome.

Previously, we investigated changes in blood coagulation and platelet activation in the coronary sinus of patients who underwent PTCA. Blood samples were drawn from the coronary sinus immediately before and after, as well as 4 and 24 hours after PTCA. Despite adequate administration of heparin and aspirin, tissue factor levels in the coronary sinus blood showed significant increases 4 and 24 hours after PTCA, and levels of thrombin-antithrombin III complex, a specific and sensitive marker for thrombin generation, also showed a significant increase 24 hours after PTCA. Furthermore, a significant positive correlation was found between changes in tissue factor levels 24 hours after PTCA and the late loss index 6 months after intervention. However, these investigators did not observe platelet activation after PTCA.

To elucidate the mechanism by which coumarin pretreatment improved outcome in BAAS, we performed an additional study (J.M. ten Berg, MD, et al, manuscript submitted for publication, 2001). Patients were randomized to aspirin alone (group A, n=26) or to aspirin plus oral anticoagulants started 1 week before PCI (group B, n=26). Unfractionated heparin (70 IU/kg) was given only during PCI. Results showed that the number of activated platelets was significantly lower before and 1 hour after PCI in group B than in group A (P<0.01 for both comparisons). In addition, the mean thrombin-antithrombin-III complex values were lower in patients pretreated with coumarins, before and until 1 day after PCI. Furthermore, patients with an international normalized ratio in the target range had significantly fewer activated platelets before and after PCI than patients with a suboptimal level of anticoagulation.

Thus, we agree with Ikeda and Shimada that the data suggest that thrombin plays a causal role in the restenosis process, which occurs despite aspirin and heparin therapy. We hypothesize, however, that anticoagulation improves outcome not only by inhibiting the coagulation pathway, but also by reducing thrombin-induced platelet activation, which is not inhibited by aspirin.

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Response

We thank Drs Ikeda and Shimeda for their interest in our recently published study. In that study and in a previously published article on the Balloon Angioplasty and Anticoagulation Study (BAAS), we demonstrated that coumarin therapy reduces both early and late thrombotic complications after percutaneous coronary intervention (PCI) when started 1 week before intervention and continued for 6 months. In addition, in patients with an optimal level of coagulation (defined as an international normalized ratio in the target range [2.1 to 4.8] for at least 70% of the follow-up time) the 6-month angiographic outcome was also significantly improved.

Others have shown that the hemostatic system is activated early after PCI and that this activation leads to a larger late loss index 6 months after intervention. However, these investigators did not observe platelet activation after PCI.

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Circulation. 2001;104:e150
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/104/24/e150

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