Direct Detection of Heparin-Induced Platelet Aggregation

To the Editor:

Enhanced platelet aggregation responses to stimulation with ADP or thrombin receptor agonist peptides (TRAP) have been observed during heparin therapy in patients with unstable angina. However, the platelet aggregation curve in Figure 3 of the article by Xiao and Théroux\(^1\) was not obtained from a direct detection to evaluate heparin-induced hyperaggregation.

A new platelet aggregometer (AG-10; Kowa, Japan) that uses a laser-light-scattering beam was introduced.\(^2\) Platelet aggregates, the size of which was measured as total voltage of light-scatter intensity at 1.0-second intervals for a 10-minute period, were divided into 3 ranges: small aggregates (diameter 9 to 25 μm), medium (26 to 50 μm), and large (>50 μm). We found that young smokers had an increased number of small platelet aggregates, which cannot be detected with a conventional aggregometer based on the turbidometric method.\(^3\) This device detects platelet aggregation in the small-aggregate size range by the addition of unfractionated heparin (UFH), and the aggregates are disaggregable in incubation with protamine sulfate. When platelet aggregation induced by UFH at a final concentration of 0.5 U/mL was observed in 36 normal subjects with no history of heparin exposure, 13 had a positive response in excess of 0.5 V of light intensity in the small-aggregate size range. In chronic hemodialysis patients in whom heparin had been used regularly for many years, a positive response with heparin-induced aggregates was noted in 37 of 59 patients, which was increased compared with that of normal subjects. The light intensity in the small-aggregate size range was enhanced during heparinized dialysis. In patients with a positive heparin response, the intensity of aggregates after heparin was significantly increased compared with that in nonresponders to heparin. Also, we obtained the same results by this system, that enhanced platelet aggregation response to heparin was not inhibited by aspirin or argatroban but was inhibited by anti-glycoprotein IIb/IIIa antibodies. The findings of enhanced platelet aggregation during heparin infusion in Figure 2 could be directly obtained without the addition of ADP or TRAP using the new device. In addition, the subjects in the article by Xiao and Théroux\(^1\) could likely have been classified into 2 groups: responders and nonresponders to heparin. The authors would have obtained clearer conclusions regarding the effect of heparin on platelets in patients with unstable angina.

Direct detection of heparin-induced platelet aggregation may be a useful method to evaluate the efficacy of heparin therapy in coronary heart disease with enhanced platelet aggregation.

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