Letter by Santos et al Regarding Article, “Pharmacodynamic Effects of Different Aspirin Dosing Regimens in Type 2 Diabetes Mellitus Patients With Coronary Artery Disease”

To the Editor:

The observation of Capodanno et al1 that increasing the frequency of administration of a low dose of aspirin has a more potent platelet inhibitory effect than increasing the daily dose of aspirin was of great interest to us because we observed a similar phenomenon several years ago in 206 patients with vascular diseases.2 It is noteworthy that although they did not observe a difference between the antiplatelet effects of once-daily (OD) and twice-daily (BID) administration of 162 mg aspirin, using the whole blood VerifyNow Aspirin test, they observed significantly lower platelet aggregation in platelet-rich plasma with BID administration than with OD administration. Cell-cell interactions in blood may have been responsible for these differences, as we have previously demonstrated that cell-cell interactions between activated platelets and intact erythrocytes significantly enhance collagen-induced platelet activation (thromboxane A2 synthesis, granule secretion) and platelet recruitment (proaggregatory activity of cell-free and collagen-free releasates).2,3 The prothrombotic effect of erythrocytes is partially inhibited by aspirin. We observed that in normal subjects, a loading dose of 500 mg aspirin supplemented daily with 50 mg of aspirin greatly reduced platelet reactivity and inhibited the prothrombotic effect of erythrocytes by 90% for 2 to 3 weeks.4 Thus, the 162 mg aspirin BID protocol used by Capodanno et al may have been insufficient to block the prothrombotic effect of erythrocytes in the whole blood test. We found that a 500-mg loading dose also suppressed the prothrombotic effect of erythrocytes in patients with vascular disease,2 but a daily dose of 50 mg aspirin was insufficient to block platelet thromboxane synthesis or [14C]-5HT release and recruitment 11 to 14 days after the loading dose. Consequently, we tested other daily aspirin regimens (50 mg BID, 100 mg OD, 100 mg BID, and 200 to 300 mg OD). Administration of 50 mg BID was more inhibitory than 100 mg OD, and 100 mg BID was more inhibitory than 50 mg BID and 200 to 300 mg OD. These results are in agreement with the observation of Capodanno et al that platelet reactivity was inhibited to a greater extent by BID administration of aspirin than by OD administration of aspirin, although we used different aspirin doses and aspirin-sensitive assay tests. However, in contrast to Capodanno et al, we also detected a decrease in platelet function when the OD dose was increased. In addition, we found that the erythrocytes of insulin-dependent diabetic patients are particularly potent in promoting platelet thromboxane synthesis and [14C]-5HT release and recruitment.5 Erythrocyte-induced enhancement of platelet function was greatest in insulin-dependent diabetic patients with poor metabolic control or long evolution times.5 These effects of erythrocytes on platelet reactivity should be taken into account to optimize the therapeutic effect of aspirin for patients with vascular disease.

Disclosures

None.

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