Warfarin Versus Aspirin in Paroxysmal Atrial Fibrillation

I read with interest the article on the relation between fibrinocoagulation activity and duration of atrial fibrillation in patients with paroxysmal atrial fibrillation by Sohara et al. (1). They concluded that anticoagulant therapy, "including suppression of platelet activity," is indicated when paroxysmal atrial fibrillation lasts for \( >12 \) h. May I point out that suppression of platelet activity is not part of anticoagulant therapy? It might also be of interest to recall the recent reports of their compatriots (2,3) on the effects of aspirin on status of thrombin generation in atrial fibrillation.

These investigators (2,3) measured plasma levels of molecular markers for platelet activity (platelet factor 4, beta-thromboglobulin) and the status of thrombin generation (thrombin–antithrombin III complex, fibrinopeptide A, F1 + 2 fragment) and fibrinolysis (t-PA, plasmin-alpha 2–plasmin inhibitor complex) before and after aspirin administration for 14 days in patients with nonvalvular atrial fibrillation. They noted that basal levels of platelet factor 4 and beta-thromboglobulin did not differ significantly between patients with atrial fibrillation and normal subjects. After 14 days of aspirin therapy, plasma levels of these markers in the patients had decreased significantly. In contrast, basal levels of fibrinopeptide A and thrombin–antithrombin III complex were significantly higher in patients with atrial fibrillation than in normal subjects. However, no significant reductions in plasma levels of these markers in the patients were observed on day 14 of aspirin treatment.

These findings thus demonstrate that thrombin activity is augmented in patients with nonvalvular atrial fibrillation. Although aspirin significantly suppressed the platelet activity, it did not affect the coagulation system. These findings also suggest that the effectiveness of aspirin in the Stroke Prevention in Atrial Fibrillation study (4) may have been due to the suppression of platelet activity, not to the suppression of thrombin generation, although they detected no increased platelet activity in patients with atrial fibrillation. Alternatively, the effectiveness of aspirin may have been due to the prevention of cerebral thrombosis, but not cardiogenic embolism. These results therefore support the premise that the administration of an anticoagulant agent is more appropriate than suppression of platelet activity by aspirin for preventing systemic embolism in patients with nonvalvular atrial fibrillation, whether chronic or paroxysmal.

References


Reply

I thank Cheng for his interest in our recent article. As he points out, aspirin significantly suppressed platelet activity but did not affect the coagulation system (1). Therefore, we agree that the sentence in the conclusion of our article, “anticoagulant therapy, including suppression of platelet activity, is required when AF [atrial fibrillation] continues for \( >12 \) h,” was ambiguous and caused misunderstanding. However, we wished to indicate that not only antithrombotic therapy but also antiplatelet therapy is important for preventing ischemic stroke, for the following reasons:

1. Disturbance of blood flow during atrial fibrillation leads to an increase in shear flow, platelet adhesion and aggregation and the release reaction. Subsequently, thrombin generation is accelerated in the presence of platelet factor 3; thrombin converts fibrinogen into fibrin; and emboil are then generated (2–4). In other words, increased platelet activity plays an important role in the primary phase of thrombus formation.

2. Yamamoto et al. (1) indicated that platelet activity in patients with atrial fibrillation was not accelerated. In contrast, some investigators have reported that it was accelerated (5–7). It is difficult to explain this discrepancy, but it may be due to differences in age or time from onset of atrial fibrillation.

3. In the Stroke Prevention in Atrial Fibrillation (SPAF-I,II) study (8,9) it was shown that warfarin may be more effective than aspirin for prevention of ischemic stroke in patients atrial fibrillation. However, younger patients had a low rate of stroke when treated with aspirin. The effectiveness of aspirin may have been due to the suppression of platelet activity. Furthermore, Yamamoto et al. (1) reported that aspirin significantly suppressed platelet function.

According to these reports, the acceleration of platelet activity in the present study may indicated that atrial fibrillation causes not only cerebral embolism but also cerebral thrombosis, and thus antithrombotic and antiplatelet combination therapy may prevent ischemic stroke more effectively. Therefore, the sentence pointed out in our article seems to be adequately expressed as “anticoagulant therapy and antiplatelet therapy is required when AF continues for \( >12 \) h.”

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References