Cardiovascular controversies

Thrombin or platelets as major point of impact in vascular reocclusion and restenosis; a controversy?

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Sometimes an apparent controversy is not that controversial on second thoughts.

In the study of factors that lead to vascular reocclusion after initial successful reperfusion, both platelets and thrombin have shown to be of significant importance. Activated thrombi are major constituents of reoccluding thrombi and secreted platelet contents appear to significantly modulate thrombus dynamics [1–3]. Alternatively, thrombin which is generated at the surface of the injured vessel or bound to the clot, may be inaccessible for physiological inhibitors and may represent the ongoing propulsive force for further activation of coagulation and thrombus formation [4]. In line with this, potent treatment strategies aimed at either inhibition of platelet activation or blocking the generation and activity of thrombin have become available and have been employed in clinical studies [5,6].

In this "controversy" the basic research findings and results of clinical studies, which are the basis for the treatment of patients with either platelet inhibitors or antithrombin agents, are highlighted in the following two outstanding papers from highly respected investigators in this field. It appears that much can be stated in favour of both treatment modalities and that experimental and clinical evidence point to an agreeable effect of both approaches. Comparative clinical trials will ultimately yield important information on which approach (or combination [7]) would be most useful in which situation and will hopefully provide more knowledge on the adverse effects of the different agents (i.e. bleeding in particular), which have to be offset against the benefits.

In both papers, however, the fact that platelets and thrombin cannot be seen as two independent quantities is underscored. Trace amounts of thrombin are potent stimuli for platelet activation and, alternatively, activation of platelets results in circumstances under which generation of thrombin is greatly facilitated. Therefore, treatment aimed towards activation of platelets will also affect generation of thrombin and potent inhibitors of thrombin will at least partly block platelet activation.

Hence, it might well be that treating platelets means (at least partly) treating thrombin and vice versa. Which means that this controversy is not that controversial on second thoughts.

References