Karolinska Institutet

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Hemostatic disturbances in acute ischemic stroke

AKADEMISK AVHANDLING
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ABSTRACT

Background: Stroke is the 2nd most common cause of death after ischemic heart disease. About 85% of all strokes are caused by a thrombus or an embolus in the cerebral circulation. Stroke causes major handicap with impaired quality of life for the patients and their families and a large costs to society. Modern treatment of ischemic stroke includes thrombolytic and antithrombotic agents, but despite this treatment many patients do suffer a new ischemic stroke.

Overall aim: To study hemostasis with emphasis on global hemostatic methods and try to identify subgroups of ischemic stroke with a more activated hemostasis, thus at risk of cerebrovascular complications.

Paper I and II: 32 patients were recruited from the Stroke units at Danderyd Hospital and at Karolinska University Hospital. Blood samples was collected in the acute phase and in the convalescence of ischemic stroke. TAFI (an attenuator of fibrinolysis), Overall Hemostatic Potential (OHP; a global marker of hemostasis assessing both coagulation and fibrinolysis) and inflammatory markers were determined in plasma. We found an impaired fibrinolysis with increased levels of TAFI and a decreased fibrinolytic capacity assessed by the OHP-method (**paper I**). Furthermore, the fibrin network formed was found to be less permeable in ischemic stroke patients (n=20) as compared to controls, both in the acute phase and after two months. In addition, the network was more resistant to fibrinolysis (**paper II**) as measured by our global method of fibrinolysis.
Paper III and IV: 209 patients with ischemic stroke (67%) or transient ischemic attack (TIA) (33%) were recruited from the Stroke units at Danderyd Hospital and at the Southern Hospital in Stockholm. Thrombin generation was measured by the Calibrated automated Thrombogram (CAT) and platelet activity was assessed by flowcytometric measurements of platelet-derived microparticles (PMPs) in plasma. Peak thrombin concentrations were found to be elevated both in the acute phase of the event and at one month (**paper III)**. In addition, an increase in PMPs was present in the acute phase and at one month. They exposed tissue factor and P-selectin on their surfaces and these molecules may contribute to the activation of hemostasis in acute ischemic stroke (**paper IV**).

Conclusion: Manifest ischemic stroke and TIA are conditions associated with an imbalance between coagulation and fibrinolysis, and elevated plasma levels of platelet-derived microparticles. Global methods of hemostasis may be useful in the evaluation of the hemostatic balance in ischemic stroke and a discrimination between high and low risk patients might be possible with standardized global assays in the future.

Keywords: ischemic stroke, acute phase, fibrinolysis, inflammation, thrombin activatable fibrinolysis inhibitor, fibrin network permeability, fibrinogen, PAI-1, fibrinolysis profile, thrombin generation, endogenous thrombin potential, cardioembolic, transient ischemic attack, paroxysmal atrial fibrillation, microparticles, tissue factor, P-selectin, flowcytometry

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