Incorporation of α2-plasmin inhibitor into fibrin clots and its association with the clinical outcome of acute ischemic stroke patients

Z. Bagoly, B. Baráth, I. Szegedi, R. Kálmándi, L. Csiba, É. Katona

Background. The cross-linking of α2-plasmin inhibitor (α2PI) to fibrin by activated factor XIII (FXIII) is essential for the inhibition of fibrinolysis. Little is known about the factors modifying α2PI incorporation into the fibrin clot and whether the extent of incorporation has clinical consequences.

Methods. α2PI activity/antigen, FXIII activity/antigen and fibrinogen levels were measured from the plasma samples of 88 individuals (62 acute ischemic stroke patients, all within 4.5 hours of their symptom onset before thrombolysis treatment and 26 age-matched healthy controls). After clotting the plasma samples by thrombin and Ca²⁺, α2PI antigen levels were measured from the serum, the extent of α2PI incorporation was calculated, and the modifying effect of FXIII levels was studied. In vitro clot-lysis experiments were performed using tissue-type plasminogen activator. In the patient cohort results were correlated with stroke severity and thrombolysis outcome.

Results. In the whole cohort FXIII levels significantly correlated with the amount of α2PI incorporation into fibrin clots (r=0.431, p=0.001). In controls and in patients with good outcomes the extent of α2PI incorporation did not differ significantly (49.2±4.2% vs. 47.4±6.7%, p=1.000). In patients suffering post-lysis intracranial hemorrhage, α2PI incorporation was significantly lower (38.1±13.8%) as compared to controls and to those with good outcomes (p=0.004 and p=0.028, respectively).

Conclusions. Increased FXIII levels result in elevated incorporation of α2PI into fibrin clots. In stroke patients the extent of α2PI incorporation seems to have an effect on the outcome of therapy, particularly on the occurrence of thrombolysis-associated intracranial hemorrhage.

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Corresponding author: Zsuzsa Bagoly
Division of Clinical Laboratory Sciences, University of Debrecen, Faculty of Medicine and MTA-DE Cerebrovascular and Neurodegenerative Research Group, Debrecen, Hungary
98 Nagyerdei krt.
Debrecen 4032, Hungary
bagoly@med.unideb.hu
phone: +36-30-2493-525