

Thrombin-activatable fibrinolysis inhibitor (TAFI) gene polymorphisms in patients with systemic sepsis ,relation to disseminated intravascular coagulation.

Abstract

Thrombin-activatable fibrinolysis inhibitor (TAFI) is a recently identified as a potent inhibitor of fibrinolysis. TAFI is activated by the thrombin-thrombomodulin complex and activated TAFI suppresses fibrinolysis by removal of carboxy-terminal lysine (and arginine) residues from partly degraded fibrin polymers, preventing the binding of the fibrinolytic components Plasminogen and tissue-type Plasminogen activator to fibrin. Recently TAFI was identified as a link between coagulation and fibrinolysis, as TAFI can be activated by thrombin and once activated potently attenuates fibrinolysis, The plasma TAFI concentration is almost entirely genetically determined, on the bases of this one would predict that DNA polymorphisms that increase TAFI activity would deteriorate the outcome of sepsis and DIC. We investigated whether plasma TAFI levels and polymorphisms located in the TAFI gene could constitute in the pathogenesis and prognosis of sepsis and DIC in 40 patients suffering from sepsis of different etiology admitted the to the Intensive Care Unit of the Cairo University and 16 normal control persons . Their baseline characteristics were similar., There was increased TAFI antigen levels in all patients however no significant difference between Patients with sepsis, severe sepsis and septic shock regarding their TAFI antigen levels [median/interquartile range (IQR) 205/35.3, 234.8/50.3, and 221.6+49.5nmol/l, respectively, p=0.543],and also DIC patients .The TAFI 325 Ile genotype (of more antifibrinolytic activity) was found in all patients on the contrary all the control person had TAFI 147 Ala of less antifibrinolytic activity .

In conclusion: The TAFI 325 Ile gene polymorphism and plasma activity was significantly high in patients with sepsis and in those with organ failure, suggesting that TAFI may play an important role in the mechanism of organ failure in DIC-associated sepsis.

Keyword : TAFI ,fibrinolysis, sepsis, DIC,thrombin ,TAFI polymorphism,MODS.