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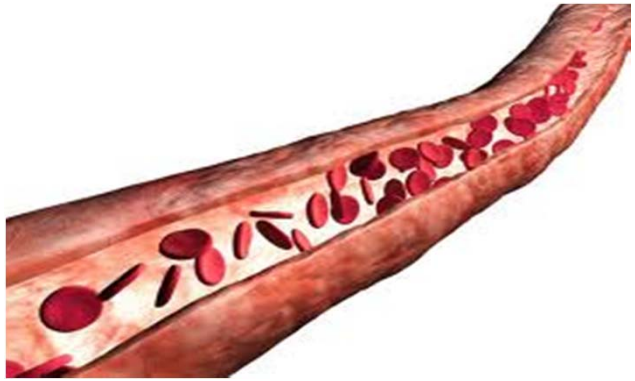
Low-grade risk of hypercoagulable state in patients suffering from diabetes mellitus type 2



Key words: Diabetes, Extrinsic coagulation pathway, Angiogenesis, Glomerular filtration rate

Introduction

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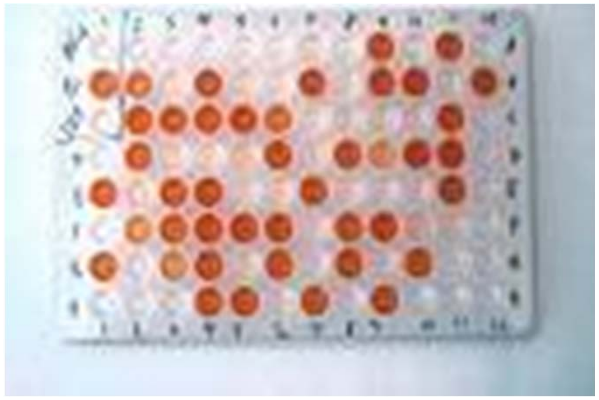
Diabetes mellitus, including type 1 and 2, is associated with the hypercoagulable state through increased thrombotic tendencies due to platelet hyper-reactivity and an increased activation of prothrombotic coagulation factors, such as VII, VIII, X, XI, XII, simultaneously with a decreased anticoagulant protein C level and the deterioration of the fibrinolysis process. These abnormalities, together with low-grade inflammation, lead to changes in the vessel architecture and the composition of the extracellular matrix (ECM)

The study was designed to evaluate changes in selected coagulation, fibrinolytic and angiogenic parameters, especially TF, TFPI, TAFI and VEGF-A in patients with diabetes mellitus type 2 (uncontrolled with microalbuminuria and well-controlled).

Methods

Sixty-two type 2 diabetes patients were enrolled in the study. Group I consisted of 27 patients having uncontrolled diabetes with microalbuminuria. The second group included 35 well-controlled diabetic patients. The control group was made up of 25 healthy volunteers. For all patients, the exclusion criteria was receiving anticoagulant-, thrombolytic therapy and antiplatelet drugs, along with Thromboembolic disease and pulmonary embolisms <6 months and surgery procedures <3 months.

- In serum were determined: VEGF-A, lipid profile and creatinine concentrations,
- In citrate plasma were measured: TF, TFPI, TAFI-Ag, plasminogen, antiplasmin, TAT complexes, and D-dimer
- In versene plasma was evaluated: HBA1c
- In fluorine plasma was determined: fasting glucose



Results

In the patients with uncontrolled diabetes, there were observed higher concentrations of TF, TFPI VEGF-A, as compared with the diabetic patients with well-controlled glycemia and control individuals. A significantly lower activity of antiplasmin was recorded in the patients with uncontrolled diabetes than in the control group.

In the patients with uncontrolled diabetes, using the multivariate regression analysis, the glomerular filtration rate were independently associated with VEGF-A, also GFR was dependently associated with total-cholesterol. Moreover tissue factors as a dependent variable were independently associated with triglycerides, HDL-cholesterol and dependently with the age. TAFI-Ag as a dependent variable was independently associated with HbA1c

Conclusions

In conclusion, serum VEGF significantly increased in the uncontrolled diabetic subjects, which is strongly related with an increased risk of the progression of vascular complications in those patients. The confirmation of this hypothesis is the relationship between VEGF-A and GFR. However, the proper control of hyperglycemia led to similar VEGF values, as compared with the control group.

The study also showed higher concentrations of TF and TFPI in the patients with uncontrolled type 2 diabetes with microalbuminuria, which is associated with the rapid neutralization of the thrombin formation, since TFPI inhibits the complex of TF/VIIa/Ca2 +. The evidence of that hypothesis is correct TAT complexes and D-dimer, which indicates a low–grade of prothrombotic risk in this group of patients. Finally, the current study suggests the role of TF in microvascular diabetic complications, which demonstrates a risk of an endothelial dysfunction, instead of the procoagulant state.