Increased Prothrombin Fragment 1 +2 in Type I Diabetic Patients

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The pathogenesis of vascular lesions in diabetic patients has been considered to be at least partly dependent on the alterations in the hemostatic system [1]. However, the existence and the relevance of a hypercoagulable state in diabetes mellitus have been the subject of much debate [1,2].

It has been demonstrated that the conversion of the coagulation zymogen prothrombin to thrombin is associated with the prominent production of a cleavage product namely prothrombin fragment 1+2 (F1+2) [3]. It has been proposed recently that prothrombin F1+2 plasma levels may be considered a very sensitive marker for hypercoagulable states in humans [4].

We evaluated prothrombin F1+2(ELISA) levels in 19 insulin-dependent diabetic patients without signs of vascular complications (12 males and 7 females: age 23.4 ± 1.9 years, mean ± SE; body mass index 22.8 ± 1.4; duration of diabetes 6.4 ± 1.3 years; insulin regimen 25-55 U/day, mean 32.8 ± 2.5 U/ day; all subjects had 24-hour urinary albumin excretion rates less than 30 µg/min, and no microaneurysms were detected on full fundal photographs or fluorescein fundal angiography; they had systolic blood pressures < 120 mm Hg and diastolic blood pressures < 90 mm Hg; ischemic heart disease and peripheral vascular occlusion were excluded according to local criteria) compared to 10 matched healthy normal subjects (6 males and 4 females: age 24.2 ± 1.8 years, body mass index 23.2 ± 1.3).

Prothrombin F1+2 levels were significantly elevated in diabetic patients (0.69 ± 0.11 vs. 0.27 ± 0.03 nmol/l;p < 0.01), but no correlation was found between prothrombin F1+2 plasma levels and both fasting glycemia (r = 0.17) and glycosylated Hb A1c (r = 0.16).

Increased FPA levels have been reported in diabetes [5]. These findings were considered more suggestive of a thrombin hyperactivity than of an increase of thrombin production [6]. This hypothesis was sustained by the evidence of normal [7] or depressed [6] levels of thrombin-antithrombin complex in the presence of increased FPA [6] and fibrin monomers [7] in diabetes.
We demonstrated that diabetic patients may have an increased thrombin production. These data are consistent with the presence of a relative hyperactivatable factor X in diabetes [8] which might explain a thrombin overproduction. Our data, moreover, support the evidence that there may be a hypercoagulable state in diabetes, even in the absence of vascular complications.

References