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DIABETES MELLITUS: HYPERCOAGULABILITY AND HYPOFIBRINOLYSIS

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A hypercoagulable state has been related to the presence of microvascular and macrovascular disease in Diabetes Mellitus. The aim of this study was to establish when this hypercoagulable state appears and the response of the fibrinolytic system.

43 patients (29 males, 14 females, aged 19-73), 28 insulin-dependent (10 of them with micro and/or macrovascular disease), 15 non insulin- dependent (all of them with vascular disease) were studied.

Platelet aggregation and adenine nucleotides, plasma and serum thromboxane B_2 (TxB_2), Factor VIII Coagulant (VIII-C), Factor VIII Related antigen (VIII-RAg), Factor VIII Ristocetin Cofactor (VIII-RCoF), Fibronectin, Tissue Plasminogen Activator (t-PA) and X-Oligomers fibrin fragments were measured.

In the diabetic patients maximal aggregation was induced by a threshold concentration of adenosin diphosphate and arachidonic acid lower than in controls ($p<0.01$ and $p<0.05$). Diabetic patients also presented elevated platelet ADP and decreased platelet c-AMP. They had higher plasma TxB_2 levels than the control group.

FVIII-C, FVIII-RAg and Fibronectin were increased ($p<0.001$) both in patients type I and II, with and without vasculopathy. FVIII-RCoF was highly increased in vasculopathy ($p<0.001$) while was non significant without it.

The patients with vasculopathy presented decreased t-PA plasma levels ($p<0.05$). No difference in X-Oligomers was found related to controls.

These findings suggest: 1) A hypercoagulable state previously to the development of clinical vasculopathy. 2) A decreased fibrinolytic response associated to vasculopathy.-

THROMBOTIC RISK FACTORS

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THROMBOSIS RISK FACTORS IN CARDIOVASCULAR SURGERY IN CHILDREN AND ADULTS.

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Antithrombin III (AT-III) and protein C (PC) deficiencies are known to be associated with a major risk of thrombosis. Before, during and after cardiovascular surgery (CS) AT-III and PC were investigated in plasma samples obtained within the framework of a randomised C1-esterase inhibitor (C1-INH)-aprotinin-placebo study in adults undergoing extracorporeal circulation (ECC), and children subjected to ECC and treated with aprotinin. Determination of AT-III and PC activity gave the following results:

AT-III: Preoperative values in adults (n = 29) and children (n = 11) were normal amounting to a median of 92 % and 100 %, respectively. In adults a steady decrease in AT-III without any difference between the 3 groups occurred during ECC until the 1st postoperative (po) day where AT-III had fallen to 78 % (median). In children the same decrease was observed during ECC, however, after termination of ECC AT-III increased until normal on the 1st day po (median = 85 %) and this difference between adults and children is significant at a p of 0.019.

Protein C: Median preoperative values in adults (n = 45) were 111 %, while in children (n = 11) only 48 % were found. During and after surgery in children there was no change in PC, while significant differences were found between the 3 adult groups. In the placebo group and the aprotinin group PC fell to 69 % (median) and 86 % (median), respectively, on the 1st day po. However, in the group receiving C1-INH Concentrate (Immuno) PC increased up to 136 % and only after discontinuation of treatment decreased to 92 % (median). The significant rise in PC in the C1-INH group is explained by the content of PC in the C1-INH Concentrate. These findings are indicative of a significant difference in the behaviour of AT-III and PC in children and adults, and suggest that the administration of C1-INH Concentrate may reduce the risk of thrombosis associated with ECC.

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ACQUIRED RISK FACTORS AND DEEP VEIN THROMBOSIS IN SYMPTOMATIC OUT PATIENTS.

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Previous studies revealed a number of acquired risk factors predisposing to acute deep vein-thrombosis (DVT). Unfortunately many of these clinical or epidemiologic studies were not proper designed, since they didn't include consecutive patients, used no or different types of objective endpoints or collected the data retrospectively. In a prospective trial we evaluated 307 consecutive out-patients with clinically suspected DVT by using ascending venography, which confirmed suspicion in 136 (44%). A history of prior thrombotic episodes as well as factors predisposing to DVT including advancing age, obesity, smoking habits, cancer, chronic lung and/or heart disease, immobilization, pregnancy, childbirth, chronic liver disease, systemic lupus erythematosus (SLE), nephrotic syndrome, varicose veins, fractures or trauma or chronic arteriopathies of the legs, diabetes mellitus (DM), recent surgery and estrogen therapy were recorded in all patients. The results of our comparison of these risk factors with the outcome of venography indicate clearly a significant difference (chi-square test) between patients with and without DVT for the following: -previous documented thromboembolism, cancer ($p < 0.01$); -chronic lung and/or heart disease, age > 65 years, immobilization ($p < 0.05$). The frequency of pregnancy, childbirth, nephrotic syndrome and chronic liver disease among our patients was too low for providing sufficiently narrow confidence limits. Surprisingly the presence of varicose veins will decrease the possibility of DVT ($p < 0.01$). In all patients (n=3) affected by SLE clinical suspicion was confirmed. Obesity, smoking habits, recent trauma or fracture or chronic artheriopathies of the legs, DM, recent surgery and estrogen therapy were not associated with an increased risk of thrombosis, since their presence in both groups was approximately the same.