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Long-term follow-up of lipid metabolism and rheologic properties after successful pancreas and kidney transplantation

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Abstract The long-term effect of pancreatic and kidney transplantation (spkt) on blood viscosity, lipid metabolism and skin microcirculation in insulin-dependent diabetes mellitus (IDDM) was studied because impaired rheological properties of blood may play a role in the development of diabetic micro- and macroangiopathy. 46 IDDM-patients (16 f/30 m; 23 ± 34 y mean duration of diabetes; 60 ± 14 mos mean follow up period) underwent spkt (Gr.I: $n = 28$) or solitary kidney (Gr. II: $n = 18$) transplantation, and were compared with healthy controls (C). Rheological measurements were performed with Mooney-Ewart rotation-viscosimeter determining whole blood viscosity (WBV), at shear rates 1, 5, 10, 20, 50, 100, 200 sec^{-1}. Triglycerides, total and HDL-, LDL- and VLDL cholesterol and fibrinogen were measured. Microcirculation was estimated by transcutaneous oxygen tension measurement ($tcpO_2$) and laser speckle method, in the forefoot area. Hemoglobin A1 was normalized only in group I (I: $7.2 \pm 0.2\%$; II: $8.3 \pm 0.3\%$; C: $< 8\%$). WBV at low shear (1, 5, 10) was increased in both groups, when compared to healthy controls (I: 12.4 ± 2; 12.5 ± 1; 6.8 ± 0.5 mpas; II: 18.7 ± 2; 13.4 ± 15; 9.4 ± 1 mpas; C: 7.5 ± 0.5; 6.7 ± 0.3; 5.4 ± 0.2 mpas; $P < 0.05$). Plasma fibrinogen was elevated in both groups compared to normals: (I: 384 ± 19; II: 448 ± 20; C: 250 ± 50 mg/dl; $P < 0.05$). There was a positive influence of spkt on skin microcirculation: $tcpO_2$/prior tx: I: 44 ± 3; II: 49 ± 6 mmHg; post tx: I: 59 ± 4; II: 42 ± 3 mmHg. Laser speckle prior tx I: 3.3 ± 0.3; II: 4.7 ± 0.2 rel. U.; post tx: 3.8 ± 0.2; II: 4.3 ± 0.2 rel. U. Patients with progression of angiopathy showed still higher fibrinogen and shear rates ($P < 0.05$). There was no significant difference for total HDL-, LDL- and VLDL cholesterol. Despite normalization of glucose metabolism and significant improvement of microcirculation in spkt patients, fibrinogen and the shear rates are increased indicating a persisting "individual" vascular risk. It is suggested that an additional hemorheological approach in the treatment posttrransplant might prevent the progression of vascular complications.

Key words Diabetes · Simultaneous kidney and pancreas transplantation
Kidney transplantation alone

Introduction

Diabetic micro- and macroangiopathy is closely linked to the long-term effects of normalized glucose metabolism. This possible beneficial effect following pancreas transplantation in type I diabetics is still under investigation [1–3]. To evaluate this relationship, a partial retrospective analysis was designed to study the effects of continuously normalized long-term glucose metabolism, changes in lipid metabolism and rheological properties of the blood as well as microangiopathy in the skin in a group of patients receiving either a kidney and a pancreas simultaneously or a kidney alone [4].

Patients and methods

Group I consisted of 28 patients with idiopathic diabetes mellitus (IDDM) who underwent simultaneous kidney and pancreas transplantation. There were 18 males and 10 females with a mean age of 36 years [range 23–56 years]. The duration of diabetes was 22 years [range 15–32 years]. Body mass index was less than 25 and duration of dialysis 26 months [range 9–37 months].

Group II consisted of 18 IDDM patients who underwent kidney transplantation alone. There were 12 male and 6 female patients with a mean age of 37 years [range 25–51 years]. The duration of diabetes was 25 years [range 19–32 years], BMI was less than 25 and duration of dialysis was 32 months [range 12–69 months]. The mean follow-up period for group I was 60 months [range 31–123 months] and for group II was 49 months [range 21–81 months]. The immunosuppressive maintenance treatment consisted on cyclosporin A (monitored on blood levels), azathioprine (50 mg/d), and prednisone (4–8 mg/d), and did not differ in both groups. All patients ate freely without any diet. No patient received lipid-lowering agents. Fasting cholesterol (TCO) and triglycerides (Tg) in plasma and lipoprotein fraction were measured by enzymatic methods, and fibrinogen (Fb) was determined by a coagulometric method (Clauss). Skin-microcirculation was estimated by transcutaneous oxygen pressure ($tcpO_2$, Kontron, Eching/Munich) and a laser speckle method (GSF Neuherberg, Munich) in the forefoot area in a comfortable supine position [5–7]. Viscosity was measured with a rotation viscometer (Mooney-Ewart, GSF Neuherberg, Munich) determining whole blood viscosity (WBV) at shear rates 1, 2, 5, 10, 20, 50, 100, 150 and 200 sec^{-1}. Statistical analysis was performed using the chi-square test and Mann-Whitney test (level of significance, $P < 0.05$, data given as mean ± SEM).

Results

There was a good metabolic control in group I (monitored by HbA1c) and good renal function in both groups. HbA1, TCO and Tg-levels were almost normal after simultaneous pancreas and kidney transplantation (values prior and post transplantation 9.16 ± 2, $7.34 \pm 2\%$; 264 ± 21, 208 ± 23 mg/dl; 246 ± 42, 146 ± 20 mg/dl) whereas group II (solitary kidney) demonstrated still higher (especially Tg) values (9.75 ± 2, $9.8 \pm 2\%$; 228 ± 16, 226 ± 17 mg/dl; 213 ± 27, 207 ± 27 mg/dl). Transplantation failed to reduce hypertriglyceridemia in group II.

Plasma fibrinogen was significantly elevated in both groups after transplantation with a significant ($P < 0.05$) difference in group II and in patients with vascular disease leading to amputation: group I, 384 ± 19, 448 ± 20; group II, 408 ± 12, 479 ± 14; all values in mg/dl). Furthermore, there was a significant difference in the lower shear rates (1, 2, 5 sec^{-1}) and whole blood viscosity demonstrating a difference not only between groups I and II, but also between patients with and without amputation in both groups (group I, 12.4 ± 2, 6.8 ± 3, 5.7 ± 0.2 mpas; group II, 18.2 ± 2, 9.3 ± 0.9, 7.6 ± 0.8 mpas; $P < 0.01$).

Group I revealed an improvement in $tcpO_2$ before transplantation, group I, $44 + 3$, group II, $49 + 6$ mmHg; after transplantation, group I, $59 + 4$, group II $42 + 3$ mgHg) and laser speckle measurement before transplantation, group I, $3.3 + 0.3$, group II, $3.8 + 0.2$ rel. U; after transplantation, group I, $5.1 + 0.3$, group II, $3.3 + 0.2$ rel. U); group II did not show a positive evaluation.

Discussion

Recent studies suggest that corticosteroids and cyclosporin are independently associated with elevated total serum cholesterol and fibrinogen levels after transplantation [8]. Total plasma cholesterol and triglyceride levels were almost normal after simultaneous pancreas and kidney transplantation, but were higher in the kidney-transplanted group. The transplantation failed to reduce the hypertriglyceridemia. Immunosuppression and hyperinsulinemia are reported as possible causes of hyperlipidemia in transplanted recipients. The raised plasma fibrinogen, together with blood hyperviscosity, may reduce blood flow not only in renal microvasculature, and elevated fibrinogen is an additional risk factor for cardiovascular complications. Despite normalization of glucose metabolism and significant improvement in microcirculation in simultaneous pancreas and kidney transplant patients, fibrinogen and shear rates at lower grades were increased, indicating a persisting individual vascular risk.

In conclusion, in this study we demonstrated that only type I diabetic patients following technically successful pancreas transplantation showed near normalization of lipid metabolism. We suggest that an additional hemorrheological approach in the posttransplant long-term treatment might prevent the progression of vascular complications. Further studies will be required to determine which of these changes are due to immunosuppressive drugs.

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