Hyperglycaemic siblings of Type II (non-insulin-dependent) diabetic patients have increased PAI-1, central obesity and insulin resistance compared with their paired normoglycaemic sibling

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Aims/hypothesis. First-degree relatives of Type II (non-insulin-dependent) diabetic patients in cross-sectional studies have increased insulin resistance, associated cardiovascular risk factors and abnormalities of fibrinolysis and coagulation. To minimise between-family genetic and environmental confounders, we investigated within-family relationships between early hyperglycaemia and risk factors.

Methods. Thirteen age and gender matched sibling pairs of Type II (non-insulin-dependent) diabetic patients, one hyperglycaemic, one normoglycaemic (fasting plasma glucose at screening 6.0-7.7 mmol l-1 and < 6.0 mmol l-1, respectively) were assessed for plasminogen activator inhibitor antigen (PAI-1), tissue plasminogen activator antigen (t-PA), fibrinogen, Factor VII and Factor VIII/von Willebrand factor antigen. Fasting lipid profiles, blood pressure and HOMA insulin sensitivity (%S) were also measured in siblings and in matched subjects without family history of diabetes.

Results. Hyperglycaemic and normoglycaemic siblings (7 female, 6 male) were aged, mean (SD) 56.8 (8.7) and 55.8 (8.4) years. Hyperglycaemic siblings had increased PAI-1 antigen, geometric mean (i.q.r.): 26.3 (15.1-45.6) vs 11.1 (2.1-23.3) ng/ml, p=0.0002, similar t-PA antigen, mean (SD) 9.5 (4.3) vs 7.4 (2.5) ng/ml, p=0.2 and fibrinogen 2.2 (0.3) vs 2.3 (0.6) g/l, p=0.5, and reduced %S 66.3 (30.5) vs 82.9 (25), p=0.04. PAI-1 correlated negatively with %S (r=-0.55, p=0.005). No significant differences were found in blood pressure or fasting lipids.

Conclusion/interpretation. A minor increase in plasma glucose in non-diabetic sibling pairs of Type II (non-insulin-dependent) diabetic patients was associated with reduced insulin sensitivity, increased central adiposity and a doubling of PAI-1 antigen concentration, suggesting impaired fibrinolysis. It is possible that this could contribute to increased cardiovascular risk in these subjects.