Observations

Subclinical inflammation in newly detected Type II diabetes and impaired glucose tolerance

To the Editor: Type II (non-insulin-dependent) diabetes mellitus, even after adjustment for established risk factors such as hypercholesterolemia, smoking and hypertension, is still associated with a higher rate (2 to 4 times) of macrovascular events than in non-diabetic subjects [1]. Obviously there are additional risk factors, which are also responsible for the accelerated atherogenesis. Subclinical inflammation was recently found to be an independent predictor of cardiovascular events [2, 3] and was also shown to be a part of the insulin resistance syndrome [4]. Since atherosclerosis starts to develop in the early stages of diabetes and in prediabetes [5, 6], it is of interest whether inflammatory parameters are also increased in newly detected Type II diabetes and in IGT. Therefore, the aim of this study was to examine C-reactive protein (CRP), leucocytes count and fibrinogen concentration in different stages of glucose intolerance.

Data were evaluated from the risk factors in IGT for atherosclerosis and diabetes (RIAD) study [6]. Briefly, 1139 subjects, aged 40 to 70 years, were included with a family history of Type II diabetes, obesity, and/or dyslipoproteinemia/hyperlipoproteinemia. Subjects with acute infections were not eligible. As lipid-lowering therapy has an anti-inflammatory effect, only participants (n = 396) without lipid lowering agents were considered for the analysis.

A standard OGTT was carried out with 75 g glucose after an overnight fast and a normal diet and physical activity for three days before the test. Subjects were classified into glucose tolerance stages according to the new ADA and WHO criteria [7, 8] – i) NGT with fasting plasma glucose (FPG) below 7.0 mmol/l and 2 h plasma glucose in OGTT below 7.8 mmol/l; ii) impaired glucose tolerance (IGT) with FPG below 7.0 mmol/l and 2 h plasma glucose in OGTT exceeding 7.8 mmol/l but below 11.1 mmol/l; iii) diabetes mellitus (DM) with FPG above 7.0 mmol/l or/and 2 h postprandial glucose concentration exceeding 11.1 mmol/l. 25 % of the examined subjects had IGT and 16 % – newly detected Type II diabetes. CRP was determined by a highly sensitive method, an immunological agglutination test (Boehringer Mannheim test kits, Mannheim, Germany) (normal values below 5.0 mg/l). Fibrinogen was measured by the method of Clauss [5] (reference range 1.50 to 4.50 g/l).

IGT and diabetic subjects showed a significantly increased leukocyte count and CRP compared with the group with NGT (Table 1). Fibrinogen concentration was significantly higher in diabetes than in NGT. The rise in inflammatory parameters parallel to the stages of glucose intolerance remained significant after adjustment for age and sex but was weakened after an additional adjustment for BMI (Table 1). It has been shown that inflammatory markers are increased in Type II diabetes [9]. In our study this was confirmed for newly detected asymptomatic diabetes with mean HbA_{1c} of only 6.3 % and also for IGT. The increased values of inflammatory parameters could be partially mediated by obesity, however they remained significantly higher even after adjustment for BMI and could therefore be an additional risk factor for atherosclerosis in the early stages of diabetes and in IGT.

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Table 1. Inflammatory parameters in newly detected Type II diabetes mellitus, impaired glucose tolerance (IGT) and normal glucose tolerance (NGT)

	NGT	IGT	Type II diabetes	p unadjusted	p age/sex adjusted	p age/sex/BMI adjusted
Fibrinogen (g/l)	3.22 ± 0.05	3.33 ± 0.10	3.66 ± 0.15[a]	IGT vs NGT NS DM vs NGT < 0.01	NS < 0.01	NS 0.05
CRP (mg/l)	2.83 ± 0.27	3.89 ± 0.40[a]	4.69 ± 0.67[a]	IGT vs NGT < 0.05 DM vs NGT < 0.01	< 0.05 < 0.01	NS 0.05
Leukocytes count (GPt/l)	5.46 ± 0 .08	5.91 ± 0.16[a]	6.33 ± 0.29[a]	IGT vs NGT < 0.01 DM vs NGT < 0.001	< 0.01 < 0.001	< 0.01 0.001

Data are means ± SEM. CRP evaluated after logarithmical transformation
[a]Significantly increased vs NGT