Blood serum levels of vascular cell adhesion molecule (sVCAM-1), intercellular adhesion molecule (sICAM-1) and endothelial leucocyte adhesion molecule-1 (ELAM-1) in diabetic retinopathy

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Abstract

Background Interaction between cells via intimate cell–cell contact is facilitated by a cell surface molecules, termed adhesion molecules. The aim of the study was to evaluate the blood serum concentration of soluble forms of vascular cell adhesion molecule (VCAM-1), intercellular adhesion molecule (ICAM-1) and endothelial leukocyte adhesion molecule-1 (ELAM-1) in patients with type 1 diabetes mellitus without and with diabetic retinopathy.

Materials and methods The study was performed in 75 patients with type 1 diabetes mellitus, 35 without retinopathy (group 1) and 40 with retinopathy (group 2). Soluble forms of VCAM-1, ICAM-1 and ELAM-1 were determined by enzyme-linked immunosorbent assay (ELISA).

Results The serum concentration of sICAM-1 and sELAM-1 were significantly elevated and the concentration sVCAM-1 was elevated but not significantly in diabetic patients when compared with control subjects. There was a significant difference in VCAM-1 concentrations between the control group and group 2 (965.9 ± 229.0 vs. 1283.7 ± 387.6 ng/ml, p < 0.05) and between group 1 and group 2 (1115.0 ± 285.5 vs. 1283.7 ± 387.6 ng/ml, p < 0.05). There were significant differences in sICAM-1 concentrations between the control group and group 1 (p < 0.05) and between the control group and group 2 (p < 0.05). Where was no significant difference in sICAM-1 concentration between group 1 and 2 (405.2 ± 135.9 vs. 443.1 ± 112.7 ng/ml, p = 0.08). ELAM-1 concentration was significantly elevated in group 2 (120.5 ± 49.3 ng/ml) when compared with the control group (51.7 ± 18.1 ng/ml, p < 0.005) and with group 1 (81.2 ± 27.7 ng/ml, p < 0.05).

Conclusions The correlations found between sVCAM-1, sICAM-1 and sELAM-1 and the presence of retinopathy suggest that cellular adhesion and neovascularization may be linked processes.

Keywords Diabetes · Diabetic retinopathy · Adhesion molecules

Introduction

Communication among cells of the immune system, and between cells of the blood–tissue barrier is a prerequisite
Diabetic retinopathy is a microvascular complication of diabetes and is closely correlated with chronic long-standing hyperglycaemia [1]. The other pathogenetic risk factors of microvascular damage in diabetes are polyp accumulation, free radical damage and nonenzymatic glycation of several proteins [2, 3].

Recent studies have demonstrated that serum levels of soluble adhesion molecules are elevated in patients with diabetes mellitus [4, 5]. Some authors have reported that the increased levels of soluble adhesion molecules play an important role in macrovascular [6–8] as well as in microvascular complications of diabetes [4, 5, 8]. Besides autoimmunological mechanisms, additional immune interactions may also be involved in the pathogenesis of microvascular complications in diabetes mellitus type 1 [9]. Diabetic retinal neovascularization is considered to be a consequence of retinal ischaemia caused by capillary occlusion. Capillary occlusion is the result of microvascular thrombi in which erythrocytes, platelets and leucocytes each may play a role. Retinal ischaemia leads to upregulation of growth factor production particularly vascular endothelial growth factor and fibroblast growth factors, and thereby induces new vessel formation in the surrounding tissue [10].

Macrovascular complications are the most common cause of early death in type 1 diabetes mellitus and microvascular complications (retinopathy) are the leading cause of visual loss in type 1 diabetes mellitus [11]. Diabetes mellitus leads to endothelial dysfunction and accelerated progression of atherosclerosis. Vascular complications of diabetes mellitus can affect not only large and medium-sized arteries resulting in coronary heart disease and peripheral artery diseases, but also small vessels leading to retinopathy and nephropathy. Raised serum levels of adhesion molecules are believed to reflect endothelial activation and may contribute to the development of diabetic vascular complications.

Adhesion molecules play an important role in the initiation and maintenance of the inflammatory immune process. Cellular activation and local expression of adhesion molecules lead to leucocyte recruitment, migration to inflammatory sites and targeting in the extravascular space [12]. Cell adhesion molecules mediate rolling and transendothelial migration of circulating leucocytes and may thus direct inflammatory cells into the intima [12]. Soluble forms of adhesion molecules are detectable in the plasma. The physiological functions of these soluble forms are unclear, but their concentrations may reflect their expression on leucocytes and endothelial cells [13, 14].

The aim of this study was to evaluate the serum concentrations of soluble forms of intercellular adhesion molecule-1 (sICAM-1), vascular adhesion molecule-1 (sVCAM-1) and endothelial leucocyte adhesion molecule-1 (sELAM-1) in patients with diabetes mellitus type 1 without and with diabetic retinopathy.

**Methods**

The study included 75 patients with type 1 diabetes (30 men, 45 women) aged from 20 to 65 years (mean ± SD 40.7 ± 11.58 years) who had been treated for more than 10 years for diabetes. After ophthalmological examination the patients were divided into the following two groups: group 1 consisted of 35 patients aged from 20 to 57 years (mean ± SD 38.9 ± 12.1 years) with a mean duration of diabetes of 17.7 ± 12.2 years, a haemoglobin A1c of 6.4 ± 1.3%, and without diabetic retinopathy; group 2 consisted of 40 patients aged from 26 to 62 years (mean ± SD 41.8 ± 10.7 years) with a mean duration of diabetes of 22.8 ± 8.6 years, a haemoglobin A1c of 6.6 ± 1.0%, and with proliferative (PDR) retinopathy. There were no significant differences in systolic and diastolic blood pressure or frequency of antihypertensive drug use between the studied groups.

The eye examination was performed by an ophthalmologist and included visual acuity, biomicroscopy and ophthalmoscopy using either a 90-dioptre lens or direct ophthalmoscopy after pupil dilatation, photography or fluorescein angiography of the retina.

Exclusion criteria were: diabetes duration less than 10 years, endocrine disease other than diabetes-related, hepatitis, and rheumatological or neoplastic diseases.

The control group consisted of 35 nondiabetic, age-matched healthy volunteers (aged from 30 to 60 years, mean ± SD 40.3 ± 9.9 years).

Blood was collected after an overnight fast, and serum was obtained by centrifugation and stored at ~70°C. Serum concentrations of sVCAM-1, sICAM-1 and sELAM-1 were determined by enzyme-linked immunosorbent assay methods. Concentrations of sICAM-1 and sVCAM-1 in serum were measured using Quantikine sICAM-1 and sVCAM-1 ELISA kits (R&D Systems, Minneapolis, MN). The sELAM-1 (CD 62E) concentration was determined using a kit from Diaclone (Besançon, France). The assays are based on a standard, sandwich ELISA technique. Serum samples were incubated on the ELISA plate precoated with specific monoclonal antibody (anti-ICAM-1, anti-VCAM-1 or anti-ELAM-1). Next, after washing, the peroxidase-labelled (sICAM-1 and sVCAM-1 kits) or biotinylated (sELAM-1 kit) monoclonal antibodies were added. Sandwich-bound biotin was detected with the Diaclone kit using strepta-