INCREASED ELASTIN TURNOVER IN OBESE AND DIABETIC CHILDREN WITH VASCULAR COMPLICATIONS

George Nicoloff¹, Chaika Petrova², Pavlina Dimitrova-Laleva³, Petkana Christova⁴

SUMMARY

The aim of the present study was to investigate the levels of elastin peptides (EP) and elastin antibodies (EA) in the sera of diabetic and obese children with vascular complications. Twenty obese hypertensive children were compared with 15 diabetic children with microangiopathy and 21 healthy nonobese children. EP and EA levels were measured using enzyme linked immunosorbent assay (ELISA). Significantly higher concentrations of EP were found in diabetic children with microangiopathy (135±41 ng/ml) and obese hypertensive children (147±41 ng/ml) than in controls (63±19 ng/ml). There was no correlation between EP and levels of IgG EA and IgM EA. However, IgE EA levels were significantly lower in control children. These data suggest an association between the activity of elastin turnover and vascular complications of diabetes mellitus and obesity.

INTRODUCTION

An important factor in the development of vascular wall alterations is degradation of the elastic fiber major protein. Elastin peptides (EP) derived from this degradation were found in circulating blood (1,2), and they act as a stimulus for the pathologically increased production of elastin antibodies (EA). Alterations in elastin structure and function lead to some pathologies of the arteries and lung (3-7). The connective tissue protein elastin is present in large amounts in the vessel wall. Both EP and EA in the circulation are good markers of the activity of elastin turnover (8-10). The aim of the present study was to measure by ELISA the levels of EP and EA (IgG, IgM and IgA) in sera of diabetic and obese children with vascular complications.

SUBJECTS AND METHODS

Subjects

Study children were divided into three groups: group I – 20 obese children with arterial hypertension (11 boys and 9 girls, mean age 12±1.3 years); group II – 15 diabetic children with microangiopathy (8 boys and 7 girls, mean age 12.3±1.4 years); and group III – 21 healthy control children (10 boys and 11 girls, mean age 11.9±1.5 years).

Enzyme-linked immunosorbent assay (ELISA)

Previously described ELISA versions (2,7) were used to study changes in the serum levels of EA and EP.
**Statistical analysis**

All values are expressed as mean±SD. Student’s t-test and ANOVA were used to assess between-group differences. The level of significance was set at p<0.05.

**RESULTS**

Significantly higher EP concentrations were found in diabetic children with microangiopathy (135±41 ng/ml) and in obese children with arterial hypertension (147±41 ng/ml) as compared to healthy controls (63±19 ng/ml) (Fig. 1). There was no correlation between EP concentration and levels of IgG and IgM determined in the same serum samples. IgA EA showed a significant increase (p<0.05) in groups I and II as compared with healthy controls (Fig. 2).

**DISCUSSION**

Epidemiologic studies have shown strong relationship between obesity and cardiovascular disease, and between obesity and specific cardiovascular risk factors such as hypertension and diabetes mellitus. In diabetic patients, morbidity and mortality are mainly related to the presence of late complications, i.e. macroangiopathy and microangiopathy. Diabetes mellitus (both type 1 and type 2) is a major risk factor for cardiovascular disease. In the Framingham Study, the risk of cardiovascular disease was doubled in the presence of diabetes (11). Obesity is also an important predictor of diabetes. A cross-sectional study in men and women showed that hypertension, hyperinsulinemia, and glucose intolerance were more pronounced in subjects with a high waist/hip ratio (12). The Nurses’ Health Study found that after adjustment for age, body mass index (BMI) was the dominant risk factor for diabetes mellitus. The risk increased with increasing BMI, and even women of average weight (BMI of 24) had an elevated risk. Compared with women of stable weight, the risk of diabetes mellitus was doubled in women who gained 5-7.9 kg after the age of 18, and trebled in those who gained 8 kg or more. These results were independent of the family history of diabetes (13). Similarly, NHANES II found that among overweight adults aged 20-75, the risk of diabetes mellitus was trebled (14). Among younger people (age 20-45), the risk was increased fourfold.

Arterial hypertension and diabetic vascular complications are connected with an elevated degradation of elastic tissue. As a result, soluble EP are
released to the circulating blood and act as a pathologic stimulus for an increased production of EA. As it is of utmost importance to identify pathologic activation of elastin turnover very early in childhood, we studied obese and diabetic children with vascular complications. Our data suggest an association between the activity of elastin turnover (especially increased serum levels of EP and IgA EA) and vascular complications of diabetes mellitus and obesity.

The relations of biological markers of extracellular matrix (plasma elastin peptides and elastase inhibitors) to the clinical history of cardiovascular diseases and risk factors for atherosclerosis were examined in 1389 men and women aged 59-71 years (15). No consistent associations were observed between either of the biological markers of extracellular matrix and age, blood pressure, BMI, and tobacco and alcohol consumption. Bako et al. (16) using DOT-immunobinding assay and \( \kappa \)-elastin isolated from bovine ligamentum nuchae, investigated middle-aged and older diabetic patients for the presence of EA. No difference was found between the number of positive and negative cases for IgM and IgG in either age group. In another study in the same group using direct ELISA and \( \kappa \)-elastin from human aorta, there were no differences in IgM EA between older diabetic patients and healthy controls, however, some elevation of IgG EA in the diabetic group was detected (8). Some discrepancies with our results could be explained by the fact that the age of study subjects, type of diabetes, and the methods and antigens used were different.

Gminski et al. (17) found the concentration of EDP to be significantly elevated in the sera of healthy children with a family history of atherosclerosis. Lindholt et al. (6) conclude from their follow-up study that serum EDP levels are a relatively strong predictor of the expansion of abdominal aortic aneurysm. The EDP concentrations found in these two studies were lower than those observed in our investigation, which may be due to methodological differences and the lack of standardization in the measurement of EDP.

REFERENCES


