ELASTIN DEGRADATION PRODUCTS AMONG OBESE CHILDREN WITH FAMILY HISTORY OF ARTERIAL HYPERTENSION

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Summary

The aim of the study was to investigate the distribution of elastin-derived proteins (EDP) in the sera of obese hypertensive children with a family history of arterial hypertension. Eighteen obese hypertensive children with a family history of arterial hypertension were compared with 23 obese nonhypertensive children with a family history of arterial hypertension, 25 obese nonhypertensive children without family history of arterial hypertension and 21 healthy nonobese children. The highest level of EDP (151±42 ng/mL) was found in obese hypertensive children with a family history of arterial hypertension, and was significantly higher than in other groups. Obese nonhypertensive children with a family history of arterial hypertension had a significantly higher EDP (92±35 ng/mL) than controls, whereas obese nonhypertensive children without family history of arterial hypertension had a significantly higher EDP (92±35 ng/mL) than controls, whereas obese nonhypertensive children without family history of arterial hypertension had a significantly higher EDP (92±35 ng/mL) than controls. These results suggest an early elastin degradation in obese children susceptible (on the basis of family history) to hypertension. Additional studies are needed to elucidate the significance of this observation.

Introduction

There are clear epidemiologic links between obesity and other cardiovascular risk factors, including hypertension, hyperlipidemia and diabetes mellitus. These effects, combined with the independent contribution of obesity itself, add up to the massive increase in the cardiovascular risk seen in obese people. Individuals with hypertension have a two- to threefold risk of coronary heart disease and sevenfold risk of stroke (1). Obesity is probably the most important modifiable risk factor contributing to hypertension, the others including alcohol consumption, dietary sodium intake and lack of physical activity (2).

Elastin, the main component of the extracellular matrix of arteries, was thought to have a purely structural role (3). Cardiovascular complications of obesity are associated with elevated degradation of elastic tissue (4). The aim of the present study was to investigate the distribution of elastin-derived peptides (EDP) in the sera of obese children with a family history of arterial hypertension.

Subjects and Methods

Subjects

Study children were divided into 4 groups, i.e. group 1: 18 children (9 boys/9 girls) aged 12.2±1.2 years, obese with arterial hypertension; group 2: 23 children (13 boys/10 girls) aged 12.6±1.1 years, obese without arterial hypertension but with a family history of arterial hypertension; group 3: 25 children (13 boys/12...
girls) aged 11.8±1.4 years, obese without data on the presence or family history of arterial hypertension; and group 4: 21 children (10 boys/11 girls) aged 11.9±1.5 years, healthy controls.

**Enzyme-linked immunosorbent assay (ELISA)**

The previously described “sandwich” version of ELISA was used to study changes in the serum levels of EDP (5).

**Statistical analyses**

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

**RESULTS**

The highest level of EDP was measured in the sera of group 1 (151±42 ng/ml), followed by group 2 children (92±35 ng/ml) (Table 1). Group 1 showed a significant increase in serum level of EDP in comparison with other groups (p<0.001). A significant increase in serum level of EDP was recorded in group 2 as compared with group 3 (p<0.01) and group 4 (p<0.01). No significant difference was found between groups 3 (69±37 ng/ml) and 4 (63±25 ng/ml) (p>0.05).

<table>
<thead>
<tr>
<th>Study group</th>
<th>EDP (ng/ml)</th>
<th>Between-group comparison</th>
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<tbody>
<tr>
<td>1</td>
<td>151±42</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>92±35</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>69±37</td>
<td>p&lt;0.001</td>
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<tr>
<td>4</td>
<td>63±26</td>
<td>p&lt;0.001</td>
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<td>(controls)</td>
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**DISCUSSION**

Obesity can result in alterations in the structure and function of the heart, irrespective of the coexistence or absence of hypertension. Additional changes occur if hypertension is also present. In obese people, peripheral resistance often decreases due to volume overload, and normal blood pressure may be maintained. However, if peripheral resistance does not change, blood pressure will rise, resulting in pressure overload of the left ventricle. This will result in concentric – as opposed to eccentric – left ventricular hypertrophy. The coexistence of obesity and hypertension has a greater effect on the left ventricular structure and function than either disorder alone (6).

The association between hypertension and obesity varies with age, being stronger in younger people. It also varies among ethnic populations (7). In the Australian Risk Factor Prevalence Study, in a predominantly Caucasian population it was estimated that obesity could account for almost one-third of hypertension in the population as a whole and for nearly two-thirds in young men (8).

That is why it would be very important to find an early marker for the development of arterial hypertension in obese children. Elastin is considered to be a stable tissue constituent with essentially no measurable turnover (9). There are, however, arguments in favor of its constant partial degradation and also for its neosynthesis (10,11). The sensitive ELISA procedure allows for determination of elastin degradation products, elastin-derived peptides in the sera of a large number of healthy and pathologic individuals (5,12-15). The relations of biological markers of extracellular matrix (plasma elastin peptides and elastase inhibitors) with 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 for either of the biological markers of extracellular matrix with age, blood pressure, body mass index and tobacco and alcohol consumption.

Arterial hypertension is connected with the loss of elasticity, increasing rigidity of the arterial wall, and an abnormal increase in the collagen/elastin ratio. As expected, we found highest elastin degradation in obese children with arterial hypertension, so-called “positive” group. However, it was more important to
study the situation in obese children free from arterial hypertension but with a family history of hypertension. The elevation of serum EDP in this group of obese children without any signs of vascular complications suggested that EDP could be used as an early marker for the development of arterial hypertension in obese children with a family history of hypertension. These results are in contrast with the EVA study (15). This contradiction with our results could be explained by differences in the age of study subjects as well as in the methods and antigens used. For example, in the EVA study an indirect ELISA with κ-elastin (as antigen for the production of antielastin antibodies for ELISA) and elderly patients were included, whereas we used α-elastin, a “sandwich-type” ELISA, and young subjects, i.e. children.

Several groups have attempted to use EDP levels in human sera as a predictor for the development of vascular disease. Gminski et al. (16) found the concentration of EDP to be significantly elevated in the sera of healthy children with a family history of atherosclerosis. In their follow-up study, Lindholt et al. (17) concluded the serum EDP levels to be a relatively strong predictor of the expansion of abdominal aortic aneurysm.

Further studies are needed to determine the clinical significance and mechanisms of this early elastin degradation in obese children with a family history of arterial hypertension.

REFERENCES
