THE PECULIARITIES OF LIPID METABOLISM AND ENDOTHELIAL DYSFUNCTION IN YOUNG PATIENTS WITH SPONDYLOGENIC VERTEBROBASILAR INSUFFICIENCY

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Abstract: To determine consistent patterns of changes of lipid metabolism and condition of an endothelium in patients of young age with the spondylogenic vertebrobasilar insufficiency we examined 98 patients (women - 56, men - 42) with manifestations of SVBI on the background of neurovascular and radicular syndromes of osteochondrosis of cervical vertebral column. Patients, age 18 to 40 years (middle age of 28.5±3.8 years) were included in this study. All study subjects underwent functional X-ray examination, cervical spine MRI and duplex scanning of neck vessels for verification diagnosis. The dynamics of blood flow indices in suboccipital (VA3) segments of vertebral and basilar arteries (BA) by dopplerography were calculated. The received data of correlation analysis confirmed the assumption of interrelation between lipid metabolism and state of an endothelium in patients with SVBI, having revealed positive correlation between the TCh level and endothelin-1 level (r = +0.58; p ≤0.05), with the same index in control group (r = +0.28; p ≤0.05). The negative correlation dependence between S-NO and LDL (r = -0.1, p≤0.05) in patient’s group was detected, in control group – (r = -0.02, p ≤0.05). Revealed in the examined patients reliable (p ≤0.05) positive correlation between the LDL level and TCh (r = +0.89) against positive correlation between the HDL level and TCh (r = +0.52) shows the sanogenetical activation of reserves in the young contingent patients and strengthening of development of an anti-atherogenous reserve. The received correlation showed that lipid metabolism plays a significant role in the promotion of endothelium dysfunction.

KeyWords: lipid metabolism, endothelial dysfunction, spondylogenic vertebra-basilar insufficiency

INTRODUCTION

Vertebrobasilar insufficiency (VBI) is a broad classification describing the condition characterized by an insufficient supply of blood via the vertebral and/or basilar arteries to the brain [14].

Blood is delivered to the brain via the carotid and vertebral arteries. The vertebral arteries are located at the back of the neck and merge at the base of the brain to form the basilar artery. The vertebral and basilar arteries supply blood to several structures in the brain including the occipital cortex, the brainstem consisting of the midbrain, pons and medulla, the cerebellum and the thalamus. As a result of decreased blood flow, the symptoms vary and are often broadly referred to as VBI or vertebral basilar ischemia.

The symptoms can include vertigo (dizziness), visual disturbances (blurring, graying, double vision), drop attack (sudden falls), numbness or tingling and slurred or lost speech. Since the portions of the brain most typically impacted are responsible for movement and balance, symptoms of VBI can often result in falls [7]. More significantly, patients with VBI are at increased risk for transient ischemic attack (TIA) and stroke. Treatable VBI may be underdiagnosed in comparison to carotid disease. Patients with vertebrobasilar ischemia do represent a significant cohort of patients. Twenty-five percent of all transient ischemic attacks and ischemic strokes involve areas of the brain supplied by the vertebrobasilar circulation. For patients who experience vertebrobasilar transient ischemic attacks, disease identified in the vertebral arteries portends a 30-35% risk for stroke over a 5-year period. Medical refractory disease of the vertebrobasilar system carries a 5-11% risk of stroke or death at 1 year. Consequently, mortality associated with a posterior circulation stroke is high,
ranging from 20-30% and this disease entity should not be ignored [5,7].

Transient ischemic symptoms referable to the posterior vascular systems are quite variable, which is consonant with the many functional systems packed into the relatively small structure of the brain stem and posterior portions of the hemispheres. These symptoms may be precipitated by rotation and hyperextension of the cervical spine which may result in temporary occlusion of the vertebral artery followed by relative ischemia at the base of the brain. This syndrome commonly presents with a combination of cerebrovascular arteriosclerosis and cervical spondylosis as fundamental clinicopathological components. [1,7]. In young patients (under 45 years) spondylogenic mechanism of VBI is more apparent, therefore the so called spondylogenic vertebrobasilar insufficiency (SVBI) is of exceptional interest.

Biochemical changes developing in patients are essential for understanding and early diagnosing of vertebrobasilar ischemia.

Interactions between blood lipid metabolism and the state of endothelium are of considerable scientific and practical interest. That is because development of endothelial dysfunction (DE) plays an essential role in vascular disorders progression.

When functioning, the endothelium involves production of biologically active agents ensuring maintenance of the vessels tone and anatomic structure, facilitating the processes of blood clot formation, regulating local inflammation [6,19]. DE can result in angiospasm, thrombi formation and adhesion of leukocytes to the endothelium. Ischemia and tissue hypoxia, hypertension, hyperglycemia, endogenous and exogenous intoxications, action of cytokines, lipid metabolism disorder, other local and general influences which strengthen death of endotheliocytes promote endothelium dysfunction and cause their defective regeneration [3,15,18].

At the same time, lipid metabolism disorders play one of the leading roles in the development of vascular complications in patients with SVBI [5,7,8,10,12,14,20]. Increased level of low density lipoproteins promotes formation of the final products of proteins oxidation and atherogenous modification of LDL also possessing cytotoxicity towards endothelial cells. Besides, hypercholesterolemia depresses formation of nitrogen oxide (NO), main vasodilatator [3,4,11,16]. The oxidized LDL promotes formation of adhesion molecules, increases smooth muscles proliferation and causes thromboses. Additionally, oxidized LDL stimulates synthesis of vasoconstrictors (endothelin-1, prostacyclin 12) and suppresses the activity of vasodilatators (serotonin, bradykinin) [1]. All the above mentioned factors contribute to endothelium dysfunction and subsequent brain blood dyscirculation [2,13].

2 PURPOSES, SUBJECTS AND METHODS:

2.1 Purpose

The aim of the study was to determine consistent patterns of changes in lipid metabolism and endothelium condition in young patients with SVBI.

2.2 Subjects

The study involved examination of 98 young patients, of them 56 women and 42 men, with signs of SVBI secondary to neurovascular and radicular syndromes of cervical osteochondrosis of the vertebral column. The study comprised patients aged 18 to 40 (middle age of 28.5±3.8 years).

2.3 Methods

All the patients underwent ultrasonic dopplerography and transcranial dopplerography of cerebral vessels with functional loading tests (head rotations) to assess spondylogenic influence on vertebral arteries. The study implied evaluation of blood flow dynamics indices in suboccipital (VA3) segments of vertebral and basilar arteries (BA) on head rotation. Velocity was estimated initially in the patients’ prone position with the head’s neutral position, then on the maximum rightwards rotation, and after that on maximum leftwards rotation. Reactivity ratio on head rotation (RR, %) was calculated by the following formula:

\[ RR = \left( \frac{V_r}{V_n} - 1 \right) \times 100 \]

\( V_r \) - Velocity in VA (BA) in the prone position
Duplex color-coded ultrasonography was used for the exclusion of atherosclerotic changes in the arteries. All study subjects underwent functional X-ray examination of the cervical vertebral column with bending and extension, cervical spine MRI, ultrasonography of the neck and head vessels with functional probes of rotation of the head, and duplex scanning of the neck vessels using the device Echocardiograf-320 (Moscow, Russia). Parameters of serum lipid metabolism were determined by spectrophotometry. The levels of total cholesterol (TCh), triglycerides (Tg) and high density lipoproteins (HDL), very low density lipoproteins (VLDL) and low density lipoproteins (LDL) indices were estimated by Friedewald’s method (Friedewald, 1972) recalculation. The study also involved calculation of atherogenic coefficient (CoA). Endothelin-1 concentration in blood serum was evaluated by immunoenzyme assay. The control group consisted of 30 gender- and age-matched healthy subjects. The obtained values were analyzed by the Student t-test. The difference was considered statistically significant at P ≤ 0.05 [9].

**Conflict of interests**

There is no conflict of interests.

### 3 RESULTS AND DISCUSSION

Doppler research showed reduction of blood velocity by 32.9% in posterior cerebral artery (PCA), by 23.1% in vertebral artery (VA) and by 23.4% in basilar artery (BA) as compared to corresponding indices in the control group. It also determined signs of vascular tone increase in the vertebrobasilar system according to the level of index pulsatility (PL) and resistance index (RL) [17] (table 1). The change in linear velocity according to the degree of head rotation was significantly higher in patients with VBI. The group was found to have variations in the number of Vr changing cases by 30% and more (P < 0.05).

Significant differences were detected during functional loading tests (head rotations) by defined reactivity ratio on rotational probe (RR). The study showed that the RR for BA in patients with SVBN was higher when compared to the control (31.0±12.2 % vs. 6.5±2.5 %) (p<0.05),

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Linear velocity of blood flow (sm/s)</th>
<th>PL, conv.units</th>
<th>RL, conv.units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SVI</td>
<td>Control</td>
<td>SVBI</td>
</tr>
<tr>
<td>ICA</td>
<td>58.1±1.95*</td>
<td>53.2±6.4</td>
<td>1.06±0.02*</td>
</tr>
<tr>
<td>ACA</td>
<td>43.1±2.3*</td>
<td>46.2±6.8</td>
<td>0.82±0.11*</td>
</tr>
<tr>
<td>PCA</td>
<td>30.1±1.8*</td>
<td>34.2±6.9</td>
<td>0.89±0.13*</td>
</tr>
<tr>
<td>VA</td>
<td>28.9±1.9*</td>
<td>37.6±7.8</td>
<td>2.39±0.15*</td>
</tr>
<tr>
<td>BA</td>
<td>35.2±2.52*</td>
<td>46.0±5.6</td>
<td>0.82±0.06*</td>
</tr>
</tbody>
</table>

Notes: * - The difference was more significant (p<0.05) when compared between the study and control groups.

The same direction was detected while analyzing RR for VA (23.4±8.2 % vs. 5.1±2.2 %) (p<0.05). Hemodynamic changes detected in the study confirmed spondylogenic influence on patients under investigation. The analysis of lipid metabolism indices in patients with SVBN revealed the disorder of transport system of lipids in all the values (Table 2).

<table>
<thead>
<tr>
<th>INDICATOR</th>
<th>Study group (n=98)</th>
<th>Controls (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCh (μmol/l)</td>
<td>5.68±0.94*</td>
<td>3.51±0.08</td>
</tr>
<tr>
<td>Tg (μmol/l)</td>
<td>0.94±0.3</td>
<td>0.78±0.06</td>
</tr>
<tr>
<td>VLDL (μmol/l)</td>
<td>0.42±0.14</td>
<td>0.26±0.04</td>
</tr>
<tr>
<td>LDL (μmol/l)</td>
<td>3.7±0.77*</td>
<td>2.02±0.07</td>
</tr>
<tr>
<td>HDL (μmol/l)</td>
<td>1.53±0.25*</td>
<td>1.14±0.03</td>
</tr>
<tr>
<td>CoA</td>
<td>2.76±0.59</td>
<td>2.14±0.09</td>
</tr>
</tbody>
</table>

Notes: * - The difference was more significant (p<0.05) when compared...
pared between the study and control groups

It was confirmed by a significant increase in TCh levels in the study group (5.68±0.94 μmol/l vs. 3.51±0.08 μmol/l). The Tg level was slightly increased as compared to the control (0.94±0.3 μmol/l vs. 0.78±0.06 μmol/l). The VLDL level was also increased in patients of the study group as compared to the control group indices (3.7±0.77 μmol/l vs. 2.02±0.07 μmol/l).

The assessment of anti-atherogenous reserve in patients under investigation showed a compensatory increase in the body defenses in terms of HDL level (1.53±0.25 μmol/l vs 1.14±0.03) (p≤0.05). Thus, a 1.3-fold increase in CoA reflected the balance of atherogenous and anti-atherogenous fractions retention in blood as evidenced by the overstrain of the body defenses, an increase in atherogenous potential of blood and, therefore, an increased risk of atherosclerosis development in the examined patients.

Moreover, the study determined an increase in the concentration of endothelin-1 as a marker of serum endothelium functional state in the study group (2.84±0.09 fentamol/ml vs. 1.25±0.08 fentamol/ml) (p≤0.05) and a decrease in S-NO level (0.18±0.07 μmol/l vs. 0.45±0.02 μmol/l). These changes confirmed vasoconstriction shift in endothelial vasoregulation.

Correlation analysis confirmed an interrelation between lipid metabolism and endothelium state in patients with SVBI, having revealed a positive correlation between TCh level and endothelin-1 (r = + 0.58; p ≤0.05), with the same index in the control group (r = + 0.28; p ≤0.05). The study group was found to have a negative correlation dependence between S-NO and LDL (r = - 0.1, p≤0.05), with (r = - 0.02, p ≤0.05) in the control group. A significant (p ≤0.05) positive correlation between LDL level and TCh (r = +0.89) revealed in the examined patients against a positive correlation between the HDL level and TCh (r = +0.52) showed a sanogenetical activation of reserves in young patients and an intensification of the anti-atherogenous reserve.

4 CONCLUSIONS

1. Development of SVBI is accompanied by lipid metabolism changes characterized by multidirectional shifts of TCh, LDL and HDL levels, confirmed by an increase in plasma indices of lipid system towards atherogenesis.

2. Endothelial dysfunction in these patients is characterized by an increased endothelin-1 concentration, being a factor of vasoconstriction opposite to a reduction of an active metabolite of nitrogen oxide - S-NO, possessing vasodilatation properties.

3. The received correlation showed that lipid metabolism plays a significant role in the promotion of endothelium dysfunction.

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