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THE DISBALANCE OF VASOACTIVE BLOOD INDICATORS IN PATIENTS WITH SPONDYLOGENIC VERTEBRA-BASILAR INSUFFICIENCY

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Abstract

Spondylogenic mechanism of circulatory insufficiency in vertebrobasilar system plays a significant role in the pathogenesis of vertebrobasilar insufficiency.

The basic metabolic indicators which define the state of cerebrovascular reactivity in patients with spondylogenic vertebra-basilar insufficiency were described in the article.

The aim of the study was to investigate the role of vasoactive substances in the formation of cerebral blood circulatory distress in young patients with spondylogenic vertebrobasilar insufficiency.

A total of 96 patients aged 25-40 years were examined and treated at the neurology department of "Kharkiv Regional Hospital – Center for emergency medical care and disaster medicine". The diagnosis of spondylogenic vertebra-basilar insufficiency was verified in the hospital according to radiographic and tomographic examination. The control group was consisted of 25 healthy volunteers matched by age.

The diagnostic complex included a survey by neurological examination, Doppler ultrasonography and biochemical research. The concentration of catecholamines in blood serum were determined by column chromatography on the columns with strongly acidic cation exchange resin "Dowex" 500w x 4 (sodium form), followed by fluorimetrical analysis. Endothelin-1 concentration was detected in serum by immune-enzymatic method and S-NO content – by spectrophotometric method.

The correlation analysis revealed a direct correlation between resistance index and the level of blood endothelin-1 ($p < 0.05$) ($r = +0.53$), which confirmed the pathogenic vasoconstrictor effect of endothelin-1 on cerebral vessels in patients with spondylogenic vertebrobasilar insufficiency. The dependence of resistance index from the level of ratio adrenaline/noradrenaline ($r = +0.39$) was also traced, which reflected a connection between the catecholaminergic disbalance and the state of vascular wall.

The clinical picture in young patients with spondylogenic vertebrobasilar insufficiency is the result of hemodynamic and metabolic factors' combined effects, among which the factors of tissue hypoxia play an important role, which is a strategically important therapeutic target in the treatment and prevention of cerebrovascular complications.

Thus, the study of endothelin-1 content and stable metabolites of nitric oxide in venous blood depending on the clinical severity of patients for pathogenically subsequent correction of revealed disorders is the perspective in the diagnosis of changes during spondylogenic vertebrobasilar insufficiency.

Keywords: *spondylogenic vertebra-basilar insufficiency, vasoactive indicators, endothelial dysfunction.*

Introduction

The features of vertebra-basilar vascular system's structure and functions, providing vital structures of brain and the originality of clinical symptoms in circulatory distress have determined its selection in the latest version of international classification as a separate symptom – "a syndrome of vertebrobasilar arterial system" under the "transient cerebral ischemic attacks and related syndromes" (ICD-10). Spondylogenic mechanism of circulatory insufficiency in the vertebrobasilar system plays a significant role in the pathogenesis of vertebrobasilar insufficiency [*Sitel A et al., 2010*]. It is known that the most common cause of pathological effects on vertebral arteries and its sympathetic autonomic plexus are vertebral arthritis, instability and intervertebral disk hernia [*Kalashnikov V, 2009*]. The disorder of cerebrovascular reactivity plays a lead-

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ing role among mediated mechanisms for the implementation of spondylogenic factors and vegetative dysfunction's negative impact on cerebral hemodynamics [*Sitel A et al., 2010*].

According to modern concepts, the dysregulation of cerebral arterial tone is determined by the expression of endothelial dysfunction [*Pushkareva T, 2008; Higashi Y et al., 2009; Chrissobolis S et al., 2011*]. It is known that endothelial dysfunction is an imbalance between the mediators, providing optimal normal endothelium during all processes. Impaired production, action and destruction of endothelial vasoactive factors are accompanied by abnormal vascular reactivity changes in the structure and growth of blood vessels [*Lishnevskaya V, 2003; Korkushko O, 2011*]. Ultimately endothelial dysfunction potentiates vasoconstriction, thrombosis, cell penetration and proliferation of macrophages that leads to the development of vascular disease [*Markov H, 2005; Vanhoutte P, 2009; Ravayeva M, 2013*].

The aim of the study was to investigate the role of vasoactive substances in the formation of cerebral blood circulatory distress in young patients with spondylogenic vertebrobasilar insufficiency.

Materials and methods

A total of 96 patients aged 25-40 years were examined at the neurology department of "Kharkiv Regional Hospital – Center for emergency medical care and disaster medicine". The diagnosis of spondylogenic vertebrobasilar insufficiency was verified in the hospital according to radiographic and tomographic examination. The control group was consisted of 25 healthy volunteers matched by age.

The complex included a survey by the neurological examination, Doppler ultrasonography (hemodynamics according to the linear flow velocity, pulsation index, and resistance index) on the unit "Spectromed-300" (Russia) and biochemical research. The concentration of catecholamines in blood serum were determined by column chromatography on the columns with strongly acidic cation exchange resin "Dowex" 500w x 4 (sodium form) 200 – 400 *mesh*, followed by fluorimetrical analysis, carried out by spectrophotometer "Hitachi-M" (Japan). The fluorescence of adrenaline was determined at wavelengths of 380/505 *nm*, norepinephrine – 395/485 *nm*. The content of endothelin -1 was determined by immunoenzyme method using ELISA – endothelin-1, the DRG company (Germany), Immunoassay Analyzer STAT – FAX 303 (USA) was used. S-NO content was measured by spectrophotometric method. [*Forstermann U, 2010; Urso C, Caimi G, 2011*].

Statistical analysis was performed using modern methods of mathematical analysis on personal computer using the statistical software package "Statistica-6". Then the average values and mean deviations were calculated. Parametric Student t-test was used as a criterion for the reliability of deviation.

Results

Conducted clinical neurological examination revealed that the major neurological syndromes in patients with spondylogenic vertebrobasilar insufficiency were vestibular syndrome (in 62 ± 4.9% of cases), which clinically manifested as transient non-systemic dizziness, occasionally accompanied by nausea, vomiting and noise in the head; syndrome of vegetative-vascular dystonia (from 68.3 ± 4.7%) and cephalic syndrome.

Cephalic syndrome (in 67.7 ± 4.8% cases) had vascular genesis. The headaches carried oppressive character, temporal or frontotemporal localization, and amplification by changing weather conditions and psycho-emotional environment. Some patients (38.7 ± 4.9%) had headache associated with intracranial hypertension with expanded character of internal pressure on the eyeballs and symptoms of hypersensitivity. In 27.5 ± 4.5% of cases headaches were caused by chronic cerebral venous circulatory distress, which was confirmed by complaints of "heaviness" in the head, "head filled with lead", daily dependence headaches (morning and early morning), the parietal-occipital region of localization, postural dependence headache (head tilt anteriorly, horizontal position of the body), as well as symptoms accompanied by headache, facial swelling, tinnitus.

Cervicocranialgia (45.9 ± 5.1%) and cervicobrachialgia were found in some patients there (23.4 ± 4.3%), which appearance can be discussed by symptomatology of periarterial nervous plexus irritation in vertebral artery. This was confirmed by the frequency and severity of pain syndromes of motor activity in the cervical spine and structural changes in this section according to X-ray and tomography.

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Muscular tonic syndrome occurred in 35.7 ± 4.8% of patients due to the irritation of pain receptors around the degenerated intervertebral discs and joints, causing excitement of spinal cord segmental apparatus and manifesting by muscle tension.

Paroxysmal states in patients with spondylogenic vertebrobasilar insufficiency observed in the form of drop attacks (in 4.1 ± 2.0% of cases), transient ischemic attacks (in 35.7 ± 4.8% of cases), syncope and vegetative paroxysms (in 10.2 ± 3.1%). Sleep disturbances were recorded in 91.6% of patients, which is probably due to the fact that the most sensitive and vulnerable distribution of adjacent circulation in vertebrobasilar system is the reticular formation of brainstem.

Central hemodynamics in patients examined according to Doppler examination was characterized by the decrease of blood flow velocity in posterior cerebral artery by 32.9%, vertebral artery 23.1% and basilar artery by 23.4% in relation to the indicators in control group. It also showed signs of increased vascular tone in the vertebra-basilar vessels according to the increase of pulsatility index and resistance index on the average 3.1 and 1.8 times (Table 1).

Coefficient of adrenaline/noradrenaline in patients with spondylogenic vertebrobasilar insufficiency was significantly higher than in the control group (0.20 ± 0.01 vs. 0.072 ± 0.002) indicating the prevalence of hormonal regulation managers and executive deficit mediators. The concentration of serotonin (Table 2) in patients with vertebrobasilar disorders was significantly higher than in the control group (0.78 ± 0.03 *mcM/l* vs. 0.45 ± 0.03), ($p < 0.05$). The obtained data showed an imbalance in the system of vasoconstrictors-vasodilators, with the prevalence of vasoconstrictors. At the same time, an increase of endothelin-1 concentration – marker of endothelial functional state in blood serum (2.84 ± 0.09 *fmol/ml* vs. 1.25 ± 0.08 *fmol/ml*) on the background of S-NO level decrease (0.18 ± 0.07 *mcM/l* vs. 0.45 ± 0.02 *mcM/l*) testified about the vasoconstrictive inclinations of endothelial vasoregulation.

Discussion

The correlation analysis revealed a direct correlation between resistance index and the level of endothelin-1 blood ($p < 0.05$) ($r = +0.53$), which confirmed the pathogenic vasoconstrictor effect of endothelin-1 on cerebral vessels in patients with spondylogenic vertebrobasilar insufficiency. The dependence of resistance index index from the level of ratio adrenaline/noradrenaline ($r = +0.39$) was also traced, which reflected a connection between the catecholaminergic disbalance and the state of vascular wall.

The clinical picture in young patients with spondylogenic vertebrobasilar insufficiency is the result

Table 1.

Hemodynamic indices of blood circulation according to the extra- and intracranial arteries

Vessels		Linear flow velocity, *sm/s*		Pulsatility index, *c.u.*		Resistance index, *c.u.*	
		Control	SVBI	Control	SVBI	Control	SVBI
Internal carotid artery	right	28.1±1.95*	53.2±6.4	1.06±0.02*	0.85±0.21	0.58±0.02*	0.55±0.16
	left	31.1±1.96*	51.9±5.9	0.95±0.06*	0.83±0.19	0.55±0.06*	0.53±0.15
Medial cerebral artery	right	53.5±5.7*	62.4±11.3	0.86±0.10*	0.56±0.14	0.52±0.15*	0.50±0.10
	left	57.2±6.2*	65.2±10.7	0.82±0.13*	0.57±0.14	0.50±0.13*	0.51±0.09
Anterior cerebral artery	right	43.1±2.3*	46.2±6.8	0.82±0.11*	0.85±0.16	0.48±0.11*	0.5±0.19
	left	41.8±2.19*	44.5±7.1	0.83±0.12*	0.83±0.14	0.51±0.09*	0.49±0.1
Posterior cerebral artery	right	30.1±1.8*	34.2±6.9	0.89±0.13*	0.86±0.17	0.55±0.06*	0.54±0.17
	left	31.6±1.67	37.1±5.3	0.87±0.12*	0.85±0.18	0.56±0.04*	0.53±0.15
Vertebral artery	right	28.9±1.98*	37.6±7.8	2.39±0.15*	0.78±0.11	0.94±0.08*	0.52±0.08
	left	29.3±2.1*	38±8.7	1.01±0.07*	0.74±0.10	0.59±0.02*	0.52±0.07
Basilar artery		35.2±2.52*	46±5.6	0.82±0.06*	0.54±0.19	0.51±0.02*	0.56±0.09

***Note**:** *$p < 0.01$ in comparison with control parameter*.

SVBI - spondylogenic vertebrobasilar insufficiency.

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TABLE 2.

The content of biogenic amines and endothelial dysfunction indicators in blood serum and in young patients with spondylogenic vertebrobasilar insufficiency

Indices	Groups	
	SVBI	Control
Serotonin (*mcM/l*)	1.04±0.03*	0.45±0.03
Adrenalin (*nM/l*)	3.65±0.27*	1.95±0.11
Noradrenalin (*nM/l*)	18.45±1.12*	26.34±1.08
Endothelin-1 (*fmol/ml*)	2.84±0.09*	1.25±0.08
S-NO (*mcM/l*)	0.18±0.07*	0.45±0.02

***NOTE*:** *p <0.05 in comparison with control parameter.SVBI - spondylogenic vertebrobasilar insufficiency.*

of hemodynamic and metabolic factors' combined effects, among which the factors of tissue hypoxia play an important role, which is a strategically important therapeutic target in the treatment and prevention of cerebrovascular complications.

It should be mentioned that in patients with spondylogenic vertebrobasilar insufficiency an imbalance occurs in the system of endothelial factors vasoregulation – nitric oxide and endothelin-1, which indicates the endothelium mechanisms of pathogenesis of present pathology, as well as an imbalance in the system of catecholaminergic vasoconstrictors – vasodilators with the prevalence of vasoconstrictors. The findings testify the dependence of vascular wall state from the level of imbalance of vasoactive substances.

Thus, the study of endothelin-1 content and stable metabolites of nitric oxide in venous blood depending on the clinical severity of patients for pathogenically subsequent correction of revealed disorders is the perspective in the diagnosis of changes during spondylogenic vertebrobasilar insufficiency.

REFERENCES

1. *Chrissobolis S, Miller AA, Drummond GR, Kemp-Harper BK, Sobey CG*. Oxidative stress and endothelial dysfunction in cerebrovascular disease. Front Biosci (Landmark Ed). 2011; 16: 1733-1745.
2. *Förstermann U*. Nitric oxide and oxidative stress in vascular disease. Pflugers Arch. 2010; 459(6): 923-939.
3. *Higashi Y, Noma K, Yoshizumi M, Kihara Y*. Endothelial function and oxidative stress in cardiovascular diseases. Circ J. 2009; 73(3): 411-418.
4. *Kalashnikov VI*. [The peculiarities of brain hemodynamics in vertebral artery syndrome in teens] [Published in Russian]. Clinical physiology of blood circulation. 2009; 3: 59-62.
5. *Korkushko OV*. [Age changes of rheological features of the blood and endothelial dysfunction of microcirculation] [Published in Russian]. Problems of aging and longevity. 2011; 1: 35-52.
6. *Lishnevskaya VY*. [Endothelial dysfunction and age] [Published in Russian]. Medical Practice. 2003; 4: 5-10.
7. *Markov HM*. [Endogenic inhibitors of nitric oxide and its place in pathology] [Published in Russian]. Russian Journal of Pediatrics. 2005; 6: 31-35.
8. *Pushkareva TA*. [The criteria of endothelial dysfunction estimation and its correction] [Published in Russian]. Clinical Laboratory Services. 2008; 5: 3-7.
9. *Ravayeva MY*. [The place of nitric oxide in the development endothelial dysfunction] [Published in Ukrainian]. Scientific notes of Tavriyskiy National Medical University. Biology, chemistry. 2013; 26(65): 147-157.
10. *Sitel AB, Kuzminov KO, Bahtadze MA*. [The influence of degenerative processes of the cervical spine on hemodynamic in the vertebrobasilar system] [Published in Russian] Manual therapy. 2010; 1(37): 10-21.
11. *Urso C, Caimi G*. [Oxidative stress and endothelial dysfunction] [Published in Italian]. Minerva Med. 2011; 102(1): 59-77.
12. *Vanhoutte PM*. Endothelial dysfunction: the first step toward coronary arteriosclerosis. Circ J. 2009; 73(4): 595-601.

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