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STRUCTURAL CHANGES OF THE VASCULAR WALL IN PATIENTS WITH CHRONIC CEREBRAL ISCHEMIA DEPENDING ON THE PRESENCE OF THE METABOLIC SYNDROME AND THE CONCENTRATION OF THE VASCULOENDOTHELIAL GROWTH FACTOR

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Abstract

Background. Chronic inflammation and enhancement of free-radical oxidation follow metabolic syndrome. Nowadays, much attention is paid to vasculoendothelial growth factor, one of the most important factors of endothelial dysfunction. There is an evidence of its possible involvement in degenerative and atherosclerotic vascular processes. **The objective:** to determine changes in the structure of the vascular wall in patients with chronic cerebral ischemia, depending on the presence of metabolic syndrome and the concentration of vasculoendothelial growth factor. **Materials and methods.** In a prospective study 49 patients with chronic cerebral ischemia were examined. The patients were randomized into 2 groups: the main group consisted of 27 patients with chronic cerebral ischemia with metabolic syndrome. There were 22 patients with chronic cerebral ischemia without metabolic syndrome in the comparison group. The severity of atherosclerotic lesions of the arteries of the head and neck was investigated taking into account the structural changes of the vascular wall, the presence of intraluminal formations, as well as their ultrasonic characteristics. In the

serum of the studied patients the concentration of vasculoendothelial growth factor was measured by enzyme-linked immunosorbent assay. **Results.** At the concentration of vasculoendothelial growth factor >300 pg/l, differentiation into layers of the intima-media complex was more often lost in patients of the main group than in patients of the comparison group: 35.7% and 0% of the examined, respectively. At this biomarker concentration, excess thickness of the intima-media complex of the common carotids (≥0.9 mm) was observed in 36.4% of patients in the main group versus 13.4% in patients in the comparison group. Also at a concentration of vasculoendothelial growth factor >300 pg/l in patients of the main group the presence of plaques was observed in 33.3%, while in patients in the comparison group plaques were not observed. **Conclusions.** Early and late manifestations of atherosclerotic structural vascular lesions in chronic cerebral ischemia with metabolic syndrome may have another quantitative biomarker of vascular endothelial damage. In these patients, the manifestations of the atherosclerotic process at all stages occur at a concentration of vasculoendothelial growth factor >300 pg/l, while atherosclerotic changes in patients without metabolic syndrome are minimal at this concentration.

Key words: chronic cerebral ischemia; cerebrovascular diseases; metabolic syndrome; ultrasound; vasculoendothelial growth factor; intima-media complex; atherosclerotic plaques.

Introduction

Cerebrovascular diseases (CVD) are one of the leading causes ofpopulation disability and mortality [1]. Chronic cerebral ischemia (CCI) is a large percentage of CVD [2]. An important role in the diagnosis of CCI is ultrasound examination of the vessels of the head and neck [1, 3]. Different stages of the atherosclerotic process can be seen in the ultrasound examination of the vessels: impaired differentiation into layers of the intima-media complex (IMC), thickening of IMC, the presence of atherosclerotic plaques (AP).

Metabolic syndrome (MS) is dangerous pathology, which doubles the risk of occurrence of cerebro- and cardiovascular diseases and risk of mortality [4, 5, 6]. The interconnection between the presence of metabolic syndrome and an increased risk of progression of the atherosclerotic process of the carotid arteries, small cerebral vessels, extra-carotid arteries, coronary arteries and abdominal aorta indicates the important role of MS in the initiation of atherosclerosis [5, 6]. Also it was found that MS is accompanied bychronic inflammation and increased free radical oxidation, and recently much attention is paid to

vasculoendothelial growth factor (VEGF), which is one of the important factors of endothelial dysfunction [7, 8].

VEGF is involved in development of metabolic syndrome at nosological level, which includes intensification of manifestations of atherosclerosis, hypertensiondisease and type 2 diabetes [8]. A number of scientific researches show the connection between concentration of VEGF with indicators of lipid metabolism and factors of inflammation [9]. There are data onpossible participation of VEGF in degenerate and atherscleroticprocesses in the vessels: development of instability of atherosclerotic plaques:nutrition of AP with its subsequent rupture and development of vascular complications [8].

The objective. To determine changes in the structure of the vascular wall in patients with chronic cerebral ischemia, depending on the presence of metabolic syndrome and the concentration of vasculoendothelial growth factor.

Materials and methods

In a prospective study 49 patients with chronic cerebral ischemia were examined. The average age of the surveyed persons was 57.08±1.12 years. The patients were randomized into 2 groups: the main group consisted of 27 patients with chronic cerebral ischemia with metabolic syndrome. There were 22 patients with chronic cerebral ischemia without metabolic syndrome in the comparison group. The severity of atherosclerotic lesions of the arteries of the head and neck was investigated taking into account the structural changes of the vascular wall, the presence of intraluminal formations, as well as their ultrasonic characteristics. The thickness of the intima-media complex of the common carotid artery and its differentiation into layers was examined by ultrasound in B-mode. IMC thickness of less than 0.9 mm was considered normal. In the serum of the studied patients the concentration of vasculoendothelial growth factor was measured by enzyme-linked immunosorbent assay.

Results of the research

The paper compared the VEGF levels concentration with changes in the structural parameters of the vascular wall in patients with CCI depending on the presence of MS and VEGF concentration.

An important indicator of changes in the morphological structure of the vascular wall was impaired differentiation into layersof the intima-media complex. Table 1 shows the incidence of preserved differentiation into layers of the intima-media complex, places of partially lost and lost differentiation depending on the presence of MS and level of VEGF concentration.

Table 1

Indicators of impaired differentiation into layers of the intima-media complex and its severity in patients with CCI depending on the presence of MS and the concentration of VEGF

Group / Indicator	Lost IMC differentiation into layers(n=22)				Preserved and partially lost IMC differentiation into layers(n=27)			
	CCI with MS (n=14)		CCI without MS (n=8)		CCI with MS (n=13)		CCI without MS (n=14)	
VEGF, pg/l	N	%	n	%	n	%	n	%
<50	3	21.4	3	37.5	2	15.4	4	28.6
50-150	2	14.3	3	37.5	1	7.7	2	14.3
150-300	4	28.6	2	25	5	38.5	4	28.6
300-500	2	14.3	0	0	3	23.1	3	21.4
>500	3	21.4	0	0	2	15.4	1	7.1

As it can be seen from the table above, differentiation into layersof the IMC in patients with CCI without MS was lost at low and medium VEGF concentrations (<300 pg/l), and in patients with MS also at high VEGF concentrations. Thus, at VEGF concentration >300 pg/l loss of differentiation into layersof the IMC was not observed in patients with CCI without MS, while the number of patients with MS and these disorders was 35.7%.

Also the study of the relationship between the IMC thicknessand VEGF concentration in patients with CCI is important for the detection of atherosclerotic lesions of the carotid arteries, depending on the presence of MS. At the same time, we determined IMC index of the common carotid arteries (CCA) at the site of its greatest thickening.

The IMC thickness of the common carotid arteries in patients with CCI depending on the presence of MS and the VEGF concentration is shown in table 2.

Table 2

IMC thickness of the common carotid arteries in patients with CCI depending on the presence of MS and VEGF concentration

Group / Indicator	IMC thickness ≥0.9 mm (n=37)				IMC thickness <0,9 mm (n=12)			
	CCI with MS (n=22)		CCI without MS (n=15)		CCI with MS (n=5)		CCI without MS (n=7)	
VEGF, pg/l	N	%	n	%	n	%	n	%
<50	5	22.7	4	26.7	0	0	3	42.9
50-150	3	13.6	5	33.3	0	0	0	0
150-300	6	27.3	4	26.7	3	60.0	2	28.6
300-500	4	18.2	1	6.7	1	20.0	2	28.6
>500	4	18.2	1	6.7	1	20.0	0	0

As seen from the table above, IMC thickness of CCA at the site of greatest thickening in patients with CCIwith MS and without MS differed depending on VEGF concentration. A significant difference in the excess IMC thickness was at high VEGF concentrations (>300 pg/l): the number of patients with CCI and MS with excess IMC thickness of the CCA (≥0.9 mm) was 36.4% versus 13.4% in patients without MS.

In this regard, we investigated the connection between the presence of atherosclerotic plaques in patients with CCI depending on the presence of MS and VEGF concentration, as shown in table 3.

Table 3

The presence of atherosclerotic plaques in patients with CCI depending on the presence of MS and VEGF concentration

Group / Indicator	With AP (n=21)				Without AP (n=28)			
	CCI with MS (n=15)		CCI without MS (n=6)		CCI with MS (n=12)		CCI without MS (n=16)	
VEGF, pg/l	N	%	n	%	n	%	n	%
<50	3	20.0	3	50.0	2	16.7	4	25.0
50-150	2	13.3	0	0	1	8.3	5	31.3
150-300	5	33.3	3	50.0	4	33.3	3	18.8
300-500	2	13.3	0	0	3	25.0	3	18.8
>500	3	20.0	0	0	2	16.7	1	6.3

As seen from table 3, an ultrasound examination of the main arteries of the head and neck among patients with CCI depending on the presence of MS revealed a difference in the occurrence of atherosclerotic plaques in the common carotid arteries at a concentration of VEGF>300 pg/l. In patients with CCI and MS, plaques were observed in 33.3% at VEGF concentration >300 pg/l, while in patients with CCI without MS at this VEGF concentration no plaques were observed. Therefore, VEGF may be one of the biomarkers of the formation of atherosclerotic plaques in patients with CCI and MS.

Due to the observed VEGF concentration-dependent deregulatory effect on vascular endothelium, cerebral ischemia progresses more actively in patients with CCI and MS. It also affects the destruction of the vascular wall of the main arteries of the head and neck and the formation of atherosclerotic plaques.

Thus, early and late manifestations of atherosclerotic structural vascular lesions in CCI and MS (IMC thickness, degree of impared differentiation into layers of the intima-media complex, atherosclerotic plaques present) may have another quantitative biomarker of vascular endothelial damage. In these patients in contrast to patients with CCI without MS,

the manifestations of atherosclerotic processes occur at VEGF concentration of >300 pg/l at all stages.In patients with CCI and no MS atherosclerotic changes were minimal at this concentration. Probably, pathological angiogenesis at an atherosclerotic process at CCI and MS has more serious consequences.

Thus, at different stages of the atherosclerotic process development VEGF is involved in patients with CCI and MS, which may affect formation of atherosclerotic plaques. Moreover, VEGF is one of the concentration-dependent biomarkers at different stages of the atherosclerotic process in patients with CCI and MS.

In these cases we suggest it is necessary to consider the VEGF concentration correction with statins, which have both hypolipidemic and anti-inflammatory properties. Also, the use of non-steroidal anti-inflammatory drugs may be appropriate in patients with CCI and MS, given the close connection of cerebral ischemia with inflammatory processes in MS, which have a pathogenic effect on vascular endothelium together with vasculoendothelial growth factor and take an active part in the pathogenesis of atherosclerotic processes.

Conclusions

1. At the concentration of vasculoendothelial growth factor >300 pg/l, differentiation into layers of the intima-media complex was more often lost in patients with chronic cerebral ischemia and metabolic syndrome than in patients with chronic cerebral ischemia without metabolic syndrome: 35.7% and 0% of the examined, respectively.

2. Excess thickness of the intima-media complex was observed at high vasculoendothelial growth factor concentration (>300 pg/l): the part of patients with chronic cerebral ischemia and metabolic syndrome with excess intima-media complex thickness of the common carotid arteries (≥0.9 mm) was 36.4% versus 13.4% in patients without metabolic syndrome.

3. For patients with chronic cerebral ischemia and metabolic syndrome, atherosclerotic plaques were present in 33.3% at vasculoendothelial growth factor concentration >300 pg/l, while in patients with chronic cerebral ischemia without metabolic syndrome no plaques were observed at this vasculoendothelial growth factor concentration.

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