

Functional Features of Vascular Endothelium with Developing Arterial Hypertension

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Abstract

At present, the initial stages of the development of vasopathy in various cardiac pathologies, especially in arterial hypertension, are of great interest to researchers. Its development negatively affects the state of the cardiovascular system, increasing the risk of thrombosis. Until now, changes in the hemostatic properties of blood vessels in a person with initial manifestations of arterial hypertension have not been adequately studied. To close the gaps in the scientific knowledge system, 65 men aged 35–45 years with arterial hypertension of the 1st degree were examined in the work. They were divided into two groups, depending on the duration of this pathology. The control group consisted of 30 healthy volunteers of the same age. In the blood of the examinees, the level of malondialdehyde, acyl hydroperoxides, catalase activity and biochemical markers of the functional state of the endothelium were determined. It was found out that, when there is an arterial hypertension of 1 degree to half a year, the violations of the measured parameters are not expressed strongly. In patients who have arterial hypertension for more than half a year, an increase in the level of tumor necrosis factor- α and a decrease in the content of nitric oxide with an increase in the manifestation of endothelial dysfunction have been noted in the blood. Apparently, these disorders progressed as a result of activation of free radical processes, which intensify as the duration of the patient's arterial hypertension increases. Strengthening of symptoms of vasopathy in patients with arterial hypertension, occurring as the duration of the disease increases, gradually increases the risk of thrombosis and thereby worsens the overall prognosis.

Keywords: Vasopathy; Arterial hypertension 1 degree; Vessels; Endothelium

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Introduction

Modern researchers pay great attention to the study of dysfunction in primary hemostasis under various pathological conditions [1,2]. It was noted that with the development of cardiac pathology, these disorders are particularly pronounced [3,4]. In this case, the dysfunction of the vascular endothelium developing in these patients is clinically very significant [5,6]. It was noticed that it progresses to a great extent due to activation of lipid peroxidation (LPO) against arterial hypertension (AH) [7], atherosclerosis [8] and metabolic pathology [9,10]. The onset of changes in the cardiovascular system inevitably leads to the development of vasopathy [11,12]. Its appearance is often associated with the development of dystrophic changes and the weakening of protein synthesis in the vascular endothelium [13, 14]. They are accelerated with increasing intensity and duration of existence of pathological processes [15], especially arterial hypertension [16,17].

Immune endothelial damage is often considered as important mechanisms of vasopathy progression, which is realized by proinflammatory cytokines-interleukin 1 β (IL-1 β), tumor necrosis factor α (TNF α) and C-reactive protein [18]. A serious manifestation

of vasopathy is the inhibition of synthesis of nitric oxide (NO) in the endothelium. To him are violations of the rheological properties of the formed blood elements [19], excessive concentration of angiotensinogen II and oxidative stress [20,21]. Acyl hydroperoxides (AGP), which are converted to malondialdehyde (MDA) during peroxidation processes, are strong mutagens and have a high cytotoxicity [22]. In addition, under conditions of intensification of free radical processes, there is an acceleration of progression of the AH itself [23,24]. At the same time, many aspects of vascular functions in the early stages of AH development remains insufficiently studied. The aim of the study is to compare the level of vascular endothelial function in patients who have the duration of their AH 1 degree to six months and more than six months.

Materials and Methods

The research was approved by the local ethical committee of the Kursk State University on September 9, 2016 (protocol №9), the local ethics committee of the Russian State Social University on September 14, 2016 (protocol №9), the local ethics committee of the Samara National Research University September 16, 2016 (protocol №9)



local ethical committee of the Samara State Agricultural Academy on October 3, 2016 (protocol №10) and the local ethics committee AllRussian Research Institute of Physiology, Biochemistry and Nutrition of Animals 07 October 2016 (protocol №10).

A total of 65 men aged 35-45 years with AH of 1 degree, risk 1-2, during the life of untreated patients on her and refused to take medication for the current time were examined. All patients were divided into 2 groups. The first group consisted of 32 patients aged 35-45 years, mean age 41.0 ± 0.9 years that had AH from 4 to 6 months. The second group consisted of 33 patients aged 35-45 years, the average age was 42.8 ± 0.6 years with an AH of 7-9 months. The control group consisted of 30 healthy volunteers who had an average age of 43.7 ± 1.2 years.

From the study excluded persons who had any clinical manifestations of atherosclerosis, autoimmune processes, metabolic disorders, cancer, and functional deficiency of the liver, kidneys and lungs.

In the work, the levels of pro-inflammatory (IL-1 β , TNF α) and antiinflammatory (interleukin-4 (IL-4)) cytokines were evaluated by means of enzyme immunoassay with the help of VECTOR BEST(Russia). The concentration of C-reactive protein in the plasma was determined by immune-turbodimetry using a set of production from the firm SRB-VITAL (Russia). The level of NO was estimated by the method of quantitative determination of total nitrite in serum using a set of production of the firm BIOCHIMMAC (Russia).

The amount of AGP in erythrocytes was determined by the method of their extraction with a heptane-isopropanol mixture. The level of MDA, catalase activity and the number of free SH groups in erythrocytes were evaluated by traditional methods. The statistical processing of the results was carried out by the STATISTICA 6.0 software package. Comparison of independent samples was carried out using the non-parametric Mann-Whitney criterion. Differences between samples were considered reliable at $p < 0.05$. Correlation analysis was also used in the work.

Results and Discussion

In the examined patients, it was noted that the index of the systemic immune reaction affecting the functions of the endothelium - the Creactive protein exceeded the normal values. In the second group of patients, he was higher than in the first.

Levels of IL 1 β , TNF α in the group of patients with AH of 1 degree, existing more than half a year, were higher than in patients with a small experience of the disease. This indicated an increase in their cytokine secretion and impaired endothelial function [25]. A more pronounced activation of the cytokine system in patients with hypertension, which existed for more than half a year, indicated higher TNF α indices- 2.2 ± 0.14 ng/ml.

In patients with a prolonged existence of hypertension, compensatory enhancement of endothelial function was noted. It was manifested by the activation of its NO-synthesizing function. Apparently, this is due to the effect of excess cytokines and active oxidative processes on the NO synthesis system in comparison with patients who have hypertension less than half a year (2.9 ± 0.20 $\mu\text{g/l}$ in the 1st group and 6.0 ± 0.29 $\mu\text{g/l}$ in the second). It may be thought that a higher level of anti-inflammatory cytokine IL-4 in patients with hypertension, which exists for more than six months, is associated with the inclusion of compensatory mechanisms stabilizing the course of the existing pathology [26].

Levels of markers of the functional state of the endothelium in the examined patients are presented in Table 1. The content of AHP and MDA in both groups of patients with AH 1 degree significantly exceeded that in the control group. At the same time, the content of MDA and AHP in the blood of persons with a prolonged course of hypertension (18.0 ± 0.09 $\mu\text{m/l}$, 41.1 ± 0.43 $\mu\text{m/l}$) exceeded the level of not only control, but also the levels of patients with a newly developed disease. The activity of the antioxidant enzyme catalase and the number of SH groups in both groups of patients were lower than in the control group. This can be explained by the high activity of LPO increasing with the increase in the length of the disease. We can assume that the severity of oxidative damage of vascular structures increases with increasing duration of hypertension of 1 degree. In this regard, it becomes clear that vasopathy almost always deepens as the duration of the disease increases. This may be due to the progression of the hypertension itself and the increase in activation of the cytokine system against the background of dysfunction of the endothelium. This assumption was confirmed by the correlation correlations revealed in the paper. Thus, in patients with AH 1 degree, existing up to six months, positive relationships between the level of NO and TNF- α were detected ($r=0.39$, $p < 0.01$); IL-4 with NO ($r=0.40$, $p < 0.01$). In patients with AH 1 degree, existing more than half a year, positive interrelations of the NO indicator with the TNF α index ($r=0.45$ $p < 0.05$) were found; TNF α and IL-4 with NO ($r=0.47$, $p < 0.01$); MDA with IL-1 β ($r=0.39$, $p < 0.05$); catalase activity with NO level ($r=0.44$, $p < 0.05$) and negative correlation of MDA concentration with Creactive protein level ($r=-0.39$, $p < 0.01$).

Conclusion

In patients with developing hypertension, LPO gradually increases, manifested by an increase in the concentration of lipoperoxidation products in plasma, while weakening its antioxidant capacity. Patients having duration of hypertension of 1 degree more than half a year have a more pronounced activity of LPO and more pronounced dysfunction of the vascular endothelium in comparison with patients who have a hypertension of 1 degree less than half a year. The revealed positive

Table 1: Considered indicators in the surveyed groups.

Indicators	1 group of patients, n=32	2 group of patients, n=33	3 control group, n=30	p 1-2	p 1-3	p 2-3
C-reactive protein, mg/l	4.5 ± 0.29	6.2 ± 0.38	3.8 ± 0.16	$p < 0.01$	$p < 0.05$	$p < 0.01$
NO, $\mu\text{g/l}$	2.9 ± 0.20	6.0 ± 0.29	2.2 ± 0.17	$p < 0.01$	$p < 0.05$	$p < 0.01$
TNF- α , ng/ml	1.4 ± 0.17	2.2 ± 0.16	1.2 ± 0.22	$p < 0.01$	$p > 0.05$	$p < 0.01$
IL 1 β , ng/ml	0.12 ± 0.02	0.22 ± 0.06	0.06 ± 0.04	$p < 0.01$	$p < 0.01$	$p < 0.01$
IL 4, ng/ml	1.2 ± 0.22	2.4 ± 0.13	0.8 ± 0.13	$p < 0.01$	$p < 0.01$	$p < 0.01$
AGP of erythrocytes, um/l	31.2 ± 0.36	41.1 ± 0.43	27.5 ± 0.51	$p < 0.01$	$p < 0.05$	$p < 0.01$
MDA of erythrocytes, um/l	12.6 ± 0.12	18.0 ± 0.09	10.5 ± 0.21	$p < 0.05$	$p < 0.05$	$p < 0.01$
SH group in erythrocytes, $\mu\text{mol/l}$	45.6 ± 0.33	41.3 ± 0.33	50.6 ± 0.35	$p < 0.05$	$p < 0.05$	$p < 0.01$
Catalase erythrocytes, $\mu\text{mol/l}$	43.8 ± 0.30	39.8 ± 0.35	46.2 ± 0.42	$p > 0.05$	$p > 0.05$	$p < 0.05$



correlation connections of LPO parameters with markers of endothelial dysfunction in patients with developing hypertension confirm the rapid increase in their functionally unprofitable changes with increasing length of disease. It becomes clear that in the development of vasopathy in this category of patients a large contribution is made by the activation of LPO, disorders in the cytokine system and the development of immune inflammation. The progression of these disorders gradually aggravates the dysfunction of the vascular endothelium, promotes the progression of hypertension and creates the basis for the development of its complications in the future.

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