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Physiological Capabilities Of The Vascular Endothelium With The Developing Arterial Hypertension In People Of Different Ages Who Had Long Had Low Physical Activity.

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ABSTRACT

Recently, the initial stages of the development of vascular pathology, including arterial hypertension, have been actively studied. It was found that the age-related changes in the cardiovascular system in many ways provide a propensity to develop arterial hypertension. The degree of age-related changes in the functional properties of the vascular endothelium in a person with beginning arterial hypertension remains insufficiently studied. We examined 77 men aged 35-73 years with grade 1 arterial hypertension, distributed according to age, into 2 groups. The control group consisted of 34 healthy mature volunteers. In their blood, the content of malonicdialdehyde, acylhydroperoxides, and Catalase and biochemical markers of endothelial function was determined. It was found that elderly patients had a higher level of tumor necrosis factor- α in the blood and a lower content of nitric oxide with more pronounced disturbances of endothelial function. Apparently, these indicators were violated by activated free radical processes, which were more pronounced than in patients of mature age. These changes largely determine in elderly patients a more severe course of arterial hypertension and a very unfavorable prognosis.

Keywords: arterial hypertension of 1 degree, vessels, endothelium, lipid peroxidation, age.

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INTRODUCTION

Recently, the study of endothelial dysfunction under different conditions has been given increasing importance [1, 2]. Development of functional disorders of the vascular endothelium is largely associated with increased lipid peroxidation (LPO), the presence of arterial hypertension (AH), atherosclerosis and metabolic disorders [3, 4]. Age-related changes in the cardiovascular system also determine the gradual development of vasopathy in humans [5, 6]. According to previous studies, age-related changes in the vascular endothelium develop gradually in proportion to the age [7, 8]. They are able to accelerate against a background of various pathological processes, including arterial hypertension [9, 10].

Among the mechanisms of progression of the vasopathia, great importance is attached to immune damage to the endothelium by proinflammatory cytokines - tumor necrosis factor α (TNF α), interleukin-1 β (IL-1 β) and C-reactive protein. Also, the disturbance of the rheological properties of the blood elements [11], the excessive concentration of angiotensinogen II and oxidative stress [12, 13], are also considered important reasons for the inhibition of the synthesis of nitric oxide (NO) by endothelium. One of the primary products of LPO is acyl hydroperoxides (AGP), which upon further oxidation are converted to malondialdehyde (MDA) [14]. Unsaturated aldehyde and MDA are mutagens and have pronounced cytotoxicity [15]. The activity of LPO in the body is limited by a whole system of antioxidants. It minimizes developing cell alteration, their dystrophy and apoptosis in all organs and especially in the vascular system [16, 17]. The intensification of free radical processes refers to the universal mechanisms of the effect of risk factors on endothelial function, contributing to the development and progression of hypertension [18]. Until now, the state of vascular functions in patients with AH at different ages, especially in conditions of prolonged hypodynamia, has not been adequately studied. The aim of the study was to study the level of oxidative processes and the state of endothelial function at grade 1 hypertension in patients of different age groups who avoided regular physical activity during their lifetime.

MATERIALS AND METHODS

The study was approved by the local ethical committee of the Kursk State University on September 15, 2016 (protocol №9) and the local ethical committee of the Kursk State Medical University on September 12, 2016 (protocol No. 9). The study was conducted on the basis of the Kursk State University and the Kursk State Medical University. We examined 77 men aged 35-73 years with AH of 1 degree, risk 1-2, during life neglected regular physical activity and had long low physical activity. The duration of AH in all patients was at least 1 year and not more than 2 years. All patients were divided into 2 groups. The first group consisted of 36 patients aged 61-73 years, with an average age of 67.2 ± 0.5 years. The second group consisted of 41 patients aged 35-60 years; the average age was 43.1 ± 0.4 years. All patients were systematically not treated for hypertension. The clinical characteristics of the examined patients are presented in Table.1. The control group consisted of 34 healthy volunteers who had an average age of 47.8 ± 1.1 years.

Table 1: Clinical characteristics of patients included in the study

Registered parameters	1 group n=36	2 group n=41	p 1-2
Duration of existence of AH, years	1.3 \pm 0.2	1.4 \pm 0.3	p>0.05
Level of systolic blood pressure, mm Hg.	146.8 \pm 1.27	149.8 \pm 2.16	p>0.05
level of diastolic blood pressure, mm Hg	97.2 \pm 0.9	98.5 \pm 1.2	p>0.05
Body mass index, kg/m ²	24.2 \pm 0.16	23.8 \pm 0.26	p>0.05

The study did not include those who had any clinical manifestations of atherosclerosis, metabolic disorders, and autoimmune processes, and ontological diseases, severe disorders of the liver, kidneys and respiratory organs.

The levels of proinflammatory (IL-1 β , TNF- α) and anti-inflammatory (IL-4) cytokines were determined by enzyme immunoassay using «VECTOR BEST» (Russia). The concentration of the C-reactive protein was

determined by the immunoturbidimetric method using the "SRB-VITAL" kit (Russia). To determine the level of NO, the method of quantitative determination of total nitrite in the serum was used with the help of the "BIOCHIMMAC" production set (Russia).

To determine the content of AHP in erythrocytes, a method of their extraction with a mixture of heptane-isopropanol was used [19]. The determination of MDA in erythrocytes was carried out according to the procedure [20]. Determination of Catalase activity in erythrocytes was carried out by the method of [21]. Free SH groups in erythrocytes were determined by the method of [18]. Statistical processing of the results was carried out using the STATISTICA 6.0 software package. For comparison of independent samples, the nonparametric Mann-Whitney criterion was used. Differences between samples were considered reliable at $p < 0.05$. Correlation analysis is used in the work.

RESULTS OF INVESTIGATION AND DISCUSSION

The baseline level of arterial pressure in both groups of patients was above the norm and corresponded to grade 1 hypertension. In the group of patients of mature age and in the group of the elderly, the ideal body weight was recorded, confirming the absence of metabolic disturbances. In all the examined patients, the indicator of the systemic immune response characterizing endothelial function-the C-reactive protein exceeded the normal values (control group) without significant differences between the compared groups.

The indices of IL-1 β , TNF- α in both groups of patients with AH of 1 degree were also higher than control ones, which may indicate an increase in cytokine secretion and endothelial dysfunction. There is reason to speak about a more pronounced activation of the cytokine system in elderly patients in comparison with patients of mature age, given their higher TNF α indices - 3.6 ± 0.12 ng / ml vs. 2.4 ± 0.16 ng / ml.

The weakening of the function of the endothelium, which manifests itself primarily in the elderly, and the decrease in its NO-synthesizing function, is associated with the effect of cytokine aggression and with the activation of oxidative processes, leading to an even greater depression of NO synthesis in comparison with patients of mature age (5.9 ± 0.19 $\mu\text{g} / \text{l}$ in the first group and 7.3 ± 0.25 $\mu\text{g} / \text{l}$ in the second group). Apparently, a greater level of anti-inflammatory cytokine IL-4 in mature patients largely determines more favorable course of hypertension and prognosis in contrast to the elderly group.

Levels of markers of the functional state of the endothelium in patients of the examined groups are presented in Table. 2. The content of AGP and MDA in both groups of patients with AH 1 degree significantly exceeded that in the control group. The MDA in elderly patients (19.2 ± 0.14 $\mu\text{M} / \text{l}$) exceeded the corresponding index in patients of mature age (15.2 ± 0.08 $\mu\text{M} / \text{l}$, $p < 0.01$); on the level of AHP, there were no differences in the groups of patients with AH of 1 degree. The content of the antioxidant enzyme Catalase and SH groups in both groups of patients was lower than in the control group, which explained the high activation of LPO in them without significant intergroup differences. Consequently, the severity of oxidative damage of vascular structures was significant in both groups of patients with AH of 1 degree, but, considering a higher level of MDA, was higher in elderly patients. This may be due to the imposition of mechanisms of the pathogenesis of hypertension on aging processes in elderly patients, which ensured more pronounced activation of the cytokine system, the existing age-related impairments of endothelial function, which was confirmed by the revealed correlation links.

In patients with AH of 1 degree of mature age, positive interrelations of the NO level with TNF- α were revealed ($r = 0.38$, $p < 0.01$); body mass index with IL-1 β ($r = 0.25$, $p < 0.05$); IL-4 with NO ($r = 0.32$, $p < 0.01$). In elderly patients positive interrelations of the NO indicator with the MDA index were revealed ($r = 0.27$ $p < 0.05$); age with a C-reactive protein ($r = 0.29$, $p < 0.01$); age with IL-1 β ($r = 0.32$, $p < 0.01$); Catalase with dynamic arterial pressure ($r = 0.25$, $p < 0.05$) and negative correlation of MDA with C-reactive protein ($r = -0.27$, $p < 0.01$).

Table 2: The indicators to be taken into account in the surveyed groups

Registered parameters	1 group of patients, n=36	2 group of patients, n=41	3group - control, n=34	p 1-2	p 1-3	p 2-3
C-reactive protein, mg/l	7.3±0.28	6.2±0.32	3.9±0.19	p>0.05	p<0.01	p<0.01
NO,mcg/l	5.9±0.19	7.3±0.25	2.1±0.14	p<0.01	p<0.01	p<0.01
TNFα, ng/ml	3.6±0.12	2.4±0.16	1.3±0.19	p<0.01	p<0.01	p<0.01
IL-1β,ng/ml	0.3±0.01	0.2±0.03	0.05±0.01	p>0.05	p<0.05	p<0.001
IL-4,ng/ml	1.3±0.26	2.2±0.17	0.9±0.10	p<0.05	p>0.05	p<0.01
AGP of erythrocytes, μM/l	47.6±0.38	51.8±0.51	28.7±0.42	p>0.05	p<0.01	p<0.01
MDA of erythrocytes, μM/l	19.2±0.14	15.2±0.08	11.1±0.16	p<0.01	p<0.01	p<0.01
SH group in erythrocytes, μmol/l	40.8±0.29	43.2±0.36	49.7±0.40	p>0.05	p<0.01	p<0.01
Catalase erythrocytes, μmol/l	38.5±0.32	40.9±0.39	45.4±0.46	p>0.05	p<0.01	p<0.05

CONCLUSION

With AH 1 degree in humans, during the life of avoiding regular physical activity, regardless of age, there is a pronounced increase in lipid peroxidation, which is an increase in lipid peroxidation products, weakening of antioxidant enzymes and development of vascular endothelial dysfunction [22, 23]. Elderly patients have more pronounced endothelial dysfunction, aggravated by activation of LPO compared to patients of mature age, which determines their less favorable prognosis. The revealed positive correlation connections of LPO indicators with markers of endothelial dysfunction in elderly patients confirm the presence of less functionally beneficial changes in them [24]. The presence of LPO activation, cytokine system and immune inflammation make a significant contribution to the formation of endothelial dysfunction in hypertension at any age. Their presence increases the age-related changes in the vascular endothelium, contributing to the unfavorable course of AH and the development of its complications in elderly patients.

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