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Signs Of The Development Of Vasopathy In Arterial Hypertension 1 Degree.

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ABSTRACT

Modern medicine seeks to study the initial manifestations of various types of pathology in order to more successfully search for means of combating it. Preservation of the prevalence in developed countries of arterial hypertension, which causes a large number of vascular complications, preserves the urgency of studies of early manifestations of this disease. Very often, the antiaggregatory properties of blood vessels are investigated, largely determining the fluid properties of blood, the duration and quality of life of patients with very common arterial hypertension. The goal is to evaluate the antiaggregatory properties of the vascular wall in patients with grade 1 arterial hypertension. The study was performed on 41 patients with arterial hypertension 1 degree of the second adult age. Control consisted of 25 healthy people of the second adulthood. Biochemical, hematological and statistical methods of investigation was used. In the patients examined, a decrease in the ant aggregative capacity of the vessels over activated platelet aggregation was found. Apparently, these disorders were caused by increased peroxide oxidation of plasma lipids, suppression of production in the walls of the vessels of nitric oxide, prostacyclin and elevation in the blood level and endothelia. In conditions of arterial hypertension of the 1st degree, the increase in aggregation properties of platelets is strongly determined by the severity of the decrease in the antiaggregational capacity of the vessel wall. The combination of these disorders greatly increases the risk of thrombosis and requires the search for options for effective correction.

Keywords: arterial hypertension 1 degrees, vascular wall, platelets, ant aggregation, second mature age, vasopathy.

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INTRODUCTION

Normally, the vascular wall completely inhibits platelet aggregation, thereby preserving blood in the liquid state [1]. This is ensured by the synthesis in the vascular endothelium of substances that exert disaggregation effects [2, 3]. It became clear that this process is very sensitive to external influences and the presence of pathology in the body. It affects, including the presence of arterial hypertension (AH). In the form of its widespread prevalence, it is increasingly being investigated [5, 6]. Its steady growth among the young population [7] and the high incidence of complications, despite ongoing treatment [8, 9], requires studies of the onset of this pathology [10]. The greatest danger of hypertension is associated with the appearance of thromboses on its background. They develop because of the weakening of synthesis in the vessels of substances that inhibit hemostasis [11]. In this regard, a very promising in terms of treatment is 1 degree of AH. In this contingent of patients, the activity of many hematological parameters is preserved [12]. In view of the relative safety of the patient's organism and the need for prevention of thrombosis in hypertension, it is very important to assess the level of vascular control over platelets at grade 1 AH [13, 14]. In this connection, the goal is to assess ant aggregation properties of the vascular wall in patients with AH of 1 degree.

MATERIALS AND METHODS

The research was approved by the Ethics Committee of Russian State Social University (record №5 from 12.05.2014).

The study was performed on 41 patients with AH 1 degree [15] second adulthood (47.0 ± 2.5 years). The criteria for inclusion in the study was the presence in patients with hypertension for at least 3 years, its compliance with the level 1 degree, patients' refusal to take medications for AH. The criteria for exclusion from the observation group were the presence of metabolic, ontological and allergic diseases. Chronic diseases of 5 persons (chronic pyelonephritis, chronic cholecystitis) were in the stage of persistent clinical remission for not less than 1.0 years. Control group was composed of 25 clinically healthy volunteers of the same age. Chronic diseases of 4 persons (chronic tonsillitis and chronic bronchitis) were in the stage of persistent clinical remission for not less than 1.5 years. All the examined persons signed the informed agreement on taking part in the investigation.

The activity of plasma lipids' peroxidation (LPO) was determined according to the content of thiobarbituricacid (TBA) – active products in it by a set "Agat-Med" (Russia) and aryl hydroperoxides (AHP) [16]. We also estimated the antioxidant potential of liquid part of blood [17]. In plasma of all the examined patients we determined the content of endothelin-1 by radioimmunological method with the help of reagents of the firm "DRG" (USA), the quantity of thromboxane A_2 metabolite – thromboxane B_2 and prostacyclin metabolite – 6-keto-prostaglandin $F_{1\alpha}$ in the course of enzymoimmunoassay with application of sets of the firm "Enzo Life Science" (USA). The summary quantity of nitric acid metabolites in blood of examined patients was determined according to the method by Metelskaya V.A. and co-authors (2005) [18]. The calculation of platelets' quantity in capillary blood was made in Goryaev's box. Platelets' aggregator ability was studied by visual micromethod [19] with the usage of the following inductors – adenosine diphosphate (ADP) (0.5×10^{-4} M), collagen (dilution 1:2 of the basic suspension), thrombin (0.125 un/ml), ristomicin (0.8 mg/ml) and adrenaline (5×10^{-6} M). The antiaggregatory activity of vascular wall was found according to AP weakening in response to all the used inductors in conditions of temporal venous occlusion. It was estimated with the help of index value of the antiaggregatory activity of vascular wall (IAAVW) which was calculated by dividing the period of AP development in plasma, received at temporal venous occlusion, on the period of AP development in blood plasma, taken without application of tourniquet on the vessel.

Statistical processing of received data was made with the help of a programmed package "Statistics for Windows v. 6.0", "Microsoft Excel". The results were processed by Student's criterion (t). Differences in data were considered reliable in case of $p<0.05$.

RESULTS AND DISCUSSION

We found strengthening of LPO in plasma: concentration of TBA-active products in it was equal to 4.61±0.019 mmol/l (in control group – 3.38±0.006 mmol/l), the content of AHP – 2.79±0.013 D_{233}/1 ml (in

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control group – 1.62±0.002 D_{233}/1ml). The examined patients had an evident weakening of antioxidant plasma activity till 28.1±0.21% (in the control group – 36.8±0.03%) (Table).

Table: The indicators considered in the surveyed

Registered parameters		Patients, n=41, M±m	Control, n=25, M±m
AHP, D_{233} /1ml		2.79±0.013	1.62±0.002 p<0.01
TBA-compounds, mcmol / l		4.61±0.019	3.38±0.006 p<0.01
plasma antioxidant activity, %		28.1±0.21	36.8±0.03 p<0.05
thromboxane A_2, pg/ml		195.1±0.47	156.5±0.66 p<0.05
6-keto-prostaglandin $F_{1\alpha}$, pg/ml		76.3±0.36	82.4±0.49 p<0.05
Total metabolites nitrogen oxide, mcmol / l		29.6±0.31	33.6±0.35 p<0.05
endothelin-1, pg/ml		14.3±0.19	8.2±0.15 p<0.01
Aggregation inductor ADP	Aggregation of platelets in intact plasma, s	36.4±0.16	42.9±0.10 p<0.05
	Aggregation of platelets in plasma after temporary venous occlusion, s	51.7±0.20	65.4±0.22 p<0.05
	IAAVW	1.42±0.007	1.52±0.012 p<0.05
Aggregation inductor collagen	Aggregation of platelets in intact plasma, s	28.0±0.12	32.4±0.04 p<0.05
	Aggregation of platelets in plasma after temporary venous occlusion, s	39.8±0.27	48.9±0.09 p<0.01
	IAAVW	1.42±0.006	1.51±0.008 p<0.05
Aggregation inductor thrombin	Aggregation of platelets in intact plasma, s	47.5±0.34	56.9±0.10 p<0.05
	Aggregation of platelets in plasma after temporary venous occlusion, s	65.1±0.42	84.2±0.12 p<0.01
	IAAVW	1.37±0.011	1.48±0.008 p<0.05
Aggregation inductorristomycin	Aggregation of platelets in intact plasma, s	39.5±0.14	45.9±0.12 p<0.05

	Aggregation of platelets in plasma after temporary venous occlusion, s	58.2±0.17	70.8±0.15 p<0.01
	IAAVW	1.47±0.008	1.54±0.009 p<0.05
Aggregation inductor adrenaline	Aggregation of platelets in intact plasma, s	80.2±0.32	99.9±0.09 p<0.05
	Aggregation of platelets in plasma after temporary venous occlusion, s	124.8±0.71	167.6±0.15 p<0.01
	IAAVW	1.55±0.004	1.68±0.010 p<0.05

Symbols: p – reliability of distinctions of indicators between a group of patients and control. In the subsequent table of designation it is similar.

In the blood of patients from the experimentalgroup, we found misbalance of arachidonic acid metabolites: the level of thromboxane B_2 rose on 24.7%, at the level lowering of its functional antagonist's derivative – 6-keto-prostaglandin $F_{1\alpha}$ on 8.0%. It was accompanied by high level of endothelin-1 in the blood (14.3±0.19 pg/ml) of examined patients and lowering of the content of summary nitric acid metabolites on 13.5% in it (Table).

The amount of platelets in patients' blood related with the normal level. AP in plasma, taken without venous occlusion, was the most accelerated one under the impact of collagen – 28.0±0.12s (in the control group – 32.4±0.04s) (table). AP developed a bit slower under the impact of ADP and ristomicin. Thrombin and adrenaline AP also developed faster than in the control group – 47.5±0.34s (in the control group – 56.9±0.10s) and 80.2±0.32s (in the control group – 99.9±0.09s), respectively (p<0.05).

In plasma, received on the background of venous occlusion, patients' AP decelerated weaker than in the group for comparison. It provided the patients with the evident lowering of IAAVW values (Table). Therefore, the maximumvalue of IAAVW was noted for adrenaline – IAAVW 1.55±0.004, whereas in the control group this value was equal to 1.68±0.010. A bit less IAAVW was registered with ristomicin and ADP. Values of IAAVW with thrombin and collagen were still lower – 1.47±0.008 and 1.42±0.007, respectively.

The onset of a persistent increase in blood pressure always adversely affects the vessels, disrupting their structure and function, creating conditions for thrombophilia [20]. At the same time, the activity of vascular hemostasis in patients with developing hypertension is still in need of clarification. The peculiarities of the basic mechanisms that can cause vasopathy in hypertension of the first degree remain unclear.

It becomes clear that the activation of peroxide oxidation of plasma lipids, which is present in AH 1, affects negatively the metabolism and the synthesis of biologically active substances in the vessels. Under these conditions, alteration of endotheliocytes increases, which weakens their functions and forms vasopathy [21].

The constantly raised level of arterial pressure registered in observed patients itself has a detrimental effect on the function of the vascular wall. This is due not only to the pronounced alteration of the endothelium, but also to the exposure of sub endothelial fibers [22]. At the same time, the synthesis of biologically active substances that inhibit platelet aggregation weakens in the vascular wall. In addition, in the platelets of these patients, the synthesis of proaggregants is enhanced [23]. This was indicated by a marked intensification of thromboxane synthesis and a decrease in prostacyclin, which created an imbalance in metabolites of arachidonic acid in their blood [24]. This leads to activation of thrombolytic thromboxane synthetase and depression of vascular prostatclylsynthetase activity. These disorders are aggravated by increased synthesis in the vessels of edothelin-1 and some weakening of the formation of nitric oxide in them.

The cause of these disorders in the patients observed is the weakening of the activity of a number of endothelial cell enzymes, enhanced by peroxide oxidation of plasma lipids [2,13].

In the course of the sample with temporal ischemia of the venous wall, weakened the ability to inhibit the adhesion of the blood platelets in patients. This happened according to two mechanisms [25]. The first mechanism is the weakening of vascular control over the number of collagen receptors-glycoproteins Ia-IIa and VI on platelets. This was indicated by a weak inhibition of AP with collagen in the plasma after temporary venous ischemia. The second mechanism of vascular attenuation of platelet adhesion in patients with AH 1 degree is associated with activation of von Willebrandfactor synthesis in the vessels and enhancement of its binding to glycoproteins IB on platelets in conditions of lack of vascular antiaggregants [26]. The increase in the amount of von Will brand factor in the blood of patients was indicated by the acceleration of AP with ristomycin, which, in its effect on platelets, is similar to sub endothelial vascular structures. Activation of von Will brand factor synthesis as a result of positive feedback stimulates an increase in the number of receptors on it on platelets, ensuring the growth of their adhesive availability [27]. An increase in the level of von Will brand factor in the plasma of patients occurs as a result of its release from the endothelium and as a result of the secretion of platelets under the influence of hemodynamic effects and active lipid peroxidation. The first mechanism of vascular control over adhesion of platelets is manifested in large arteries and veins, the second - in conditions of blood flow in small vessels [27,28].

In conditions of reduced synthesis in the walls of the vessels of physiological disaggregates with AH of 1 degree, fixation of strong agonists of aggregation - collagen and thrombin - to their receptors on platelets increases. This leads to activation of phospholipase C and stimulation of the phosphoinositol pathway with phosphorylation of actin and myosin. Synthesized excess of instill triphosphate leads to the release of Ca^{2+} from the intra-platelet depot, stimulating the contraction of actin and myosin relative to each other [29]. Weak aggregation inducers ADP and adrenaline also actively combine with their receptors on platelet membranes. When there is a lack of synthesis in the vessels of prostacyclin and nitric oxide, fibrinogen receptors (glycoproteins IIb-IIIa) develop and phospholipase A_2 is activated. This leads to an increase in the yield of phospholipids from platelets of arachidonic acid. Under these conditions, activated by metabolic disturbances and enhanced lipid peroxidation of cyclooxygenase lipids and thromboxane synthetase of platelets generate a lot of thromboxane A_2. In physiological conditions, thromboxane A_2 and products of the instill pathway can stimulate the release of a prostacyclin vessel that inhibits the activity of thromboxane A_2 [30]. However, even with AH 1 degree secretion from the vessels of these substances begins to weaken and does not completely compensate for the effect of proaggregants. It is likely that the onset of hemodynamic disorders and increased lipid peroxidation in the plasma form vasopathy in these patients.

CONCLUSION

Patients with AH 1 degree had an increase in platelet aggregation, which was combined with a decrease in the ant aggregative capacity of the vessel wall. At the heart of these disorders, apparently, is the activation of peroxide oxidation of plasma lipids. It leads to an imbalance in the blood of metabolites of arachidonic acid, increased synthesis in the wall of vessels of von Will brand factor and the weakening of the formation of NO in it. These disorders are very important in terms of formation of a risk of thrombosis in the examined category of patients.

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