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Possibilities Of Combined Therapy In Relation To Disaggregation Parameters Of Blood Vessels In Patients With Metabolic Syndrome With A High Degree Of Arterial Hypertension.

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ABSTRACT

There is no doubt that patients with a high degree of arterial hypertension in the metabolic syndrome need a comprehensive correction aimed at the maximum possible elimination of all their violations. The goal is to establish the severity of the dynamics of antiaggregatory ability of the vessel wall in patients with arterial hypertension of 3 degrees in the metabolic syndrome on the background of pathogenetically justified complex therapy. Available in the examined 24 patients with complicated hypertension 3 degrees in the metabolic syndrome excessive platelet activity detected in vitro and in vivo is based on improving their adhesion and aggregation activity due to coming in their blood imbalance of Pro - and antiaggregatory effects. The most significant causal factors of this situation should be considered, such as arterial hypertension, adverse changes in the lipid composition of the plasma and the enhancement of lipid peroxidation. Therapy, including amlodipine, valsartan, pioglitazone, a low-calorie diet and dosed physical load, after 4 months provides in patients with arterial hypertension of 3 degrees in the metabolic syndrome persistent normalization of the initial high activity of platelets and reduced vascular control over it despite subsequent imperfect adherence to non-pharmacological component of complex effects.

Keywords: vascular wall, antiaggregative, platelets, arterial hypertension, metabolic syndrome, integrated therapy.

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INTRODUCTION

Until now, in developed countries, one of the leading places in the development of complications and deaths in the structure of the overall incidence belongs to cardiovascular pathology [1,2]. In this case, a very large proportion of it has arterial hypertension (AH) and its complications, which have pronounced negative effects on the cardiovascular system and significantly increase the risk of thrombosis [3,4]. It was noted that the addition of various metabolic disturbances [5] and especially the metabolic syndrome (MS), including hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, abdominal obesity, insulin resistance, manifested either by impaired glucose tolerance or diabetes mellitus, additionally sharply increases the risk of developing cardiovascular catastrophes [6, 7]. This is largely due to the fact that people with MS who have hypertension have a high degree of platelet activation and a decrease in the hemostatic properties of blood vessels, which significantly increases the risk of thrombosis of different localization [8,9].

There is no doubt that patients with a high degree of hypertension with MS need a comprehensive correction aimed at the maximum possible elimination of all their violations [10,11]. According to modern views, this combination of patients is pathogenetically justified by the use of a combination of modern and safe antihypertensive drugs (angiotensin receptor blockers, for example, valsartan and calcium antagonists, for example, amlodipine), a hypoglycemic drug (eg, pioglitazone) and non-drug therapy, including rational diet and physical loads [12, 13]. In this connection, the effect of this complex on the important mechanism of formation and maintenance of thrombophilia is of great scientific and practical interest-high platelet activity and individual mechanisms controlling it in patients with AH of grade 3 in MS [14,15].

In this regard, the goal of the study was formulated: to establish the severity of the dynamics of the antiaggregative capacity of the vascular wall in patients with AH of grade 3 with MS on the background of pathogenetically justified complex therapy.

MATERIAL AND METHODS

The conducted research was approved by the Local Ethic Committee of the Russian State Social University in May,17th, 2016 (Record №5). The study included 24 patients with AH of 3 degrees, risk 4, including 10 men and 14 women of mature age (49.1±1.9 years). All patients had a combination of AH with a diagnosis in strict accordance with the generally accepted criteria of MS, consisting of a violation of glucose tolerance, hyperlipidemia II b type, abdominal obesity (body mass index more than 30 kg/m^2, the ratio of waist volume to hip volume more than 0.85 in women and more than 1.0 in men). The control group consisted of 25 clinically healthy people of similar age. A group of patients and a group of healthy people had a normal amount of platelets in their blood.

The blood in both groups was taken after 14 hours of starvation. The content of total cholesterol, high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) was determined by the enzymatic colorimetry method using the Vital Diagnosticum kit, the total lipids concentration was determined using the Erba Russ kit. The low-density lipoprotein cholesterol (LDL) cholesterol was calculated according to the Friedwald formula, the cholesterol-lower density lipoprotein cholesterol (VLDL) was calculated by the formula: TG / 2.2 content. The lipid composition was evaluated in full accordance with the Russian recommendations on the diagnosis and correction of lipid metabolism disorders [16].

The activity of lipid peroxidation (LPO) of plasma was detected by the content of thiobarbituric acid (TBA) -active products by a set of Agat-Med and acyl hydroperoxides (AGP) [17]. In all patients, the antioxidant potential of the liquid part of the blood was determined [18].

All the subjects surveyed in the plasma determined the endothelin-1 content by radioimmunoassay using DRG reagents (USA), as well as the levels of thromboxane A2 thromboxane B2 metabolite and prostacyclin metabolite 6-keto-prostaglandin F1α by enzyme immunoassay using the " Enzo Life science »(USA). The total content of the observed nitric oxide metabolites in the blood was determined by the method of VA Metelskaya. et al. (2005) [19].

Aggregation of platelets (AP) was evaluated on a two-channel laser analyzer aggregation of platelets ALAT2- "BIOLA" (model LA230-2, Russia) using as inductors ADP (0.5×10^{-4} M), collagen (1: 2 dilution of the

basic suspension), ristomycin (0.8 mg / ml). Intravascular activity of thrombocytes (BAT) was determined with phase contrast. The antiaggregatory activity of the vascular wall was determined in a sample with temporal venous occlusion by inhibition of BAT and attenuation of AT with calculation of the platelet aggregation index (ISTAT) by dividing the degree of aggregation without cuff to the degree of platelet aggregation with it and calculating the platelet aggregation index (IPAT) aggregation without overlapping the cuff to the aggregation index with cuff.

In order to correct blood pressure (BP) patients were prescribed amlodipine 10mg once a day and valsartan 160mg once a day, to optimize carbohydrate metabolism - pioglitazone at a dose of 30 mg once a day. Non-pharmacological therapy included a hypocaloric diet and feasible regular physical training. Evaluation of clinical and laboratory indicators was carried out at the time of taking and at 2, 4, 12 and 36 months of therapy. The non-compliance with the non-pharmacological component of the ongoing correction was allowed after 4 months. treatment.

Statistical processing of the obtained results was carried out using Student's t-test.

RESEARCH RESULTS

The initial level of arterial pressure in the patients under observation (systolic - 186.1±4.3 mm Hg, diastolic - 114.8±3.2 mm Hg) corresponded to grade 3 hypertension. After 2 weeks of therapy, the blood pressure level in the observed patients stabilized at the level: systolic - 135.0±2.1 mm Hg, diastolic - 85.3±1.3 mm Hg. and remained at the achieved level until the end of the observation.

In the blood of patients, increased amounts of OL and OXC prevailed over control values of 1.67 and 1.30 times, respectively (Table 1). At the same time, in the blood of the observed persons with AH of grade 3, MS also showed an increase in LDL cholesterol, cholesterol VLDL and TG in 1.52, 1.68 and 1.67 times, respectively, combined with a decrease in HDL cholesterol 1.32 times. Against this background, the expressed activation of plasma LPL was revealed in the patients - the content of AGP in it (3.70 ± 0.003 D_{233}/1 ml) exceeded the control 2.28 times, TBA-active products (5.80 ± 0.003 μmol / l) - in 1.71 times with a decrease in the value of the antioxidant potential of the liquid part of the blood by 79.5%.

As a result of the use of complex therapy in the blood of patients there was a gradual decrease in the levels of OL and OXC, reaching the control values after 4 months. (Table 1). This was accompanied in the observed patients by a decrease in their plasma concentrations of LDL, LLDPE and TG cholesterol and an increase in HDL cholesterol to the control figures at 4 months. with their subsequent stabilization at the achieved level until the end of the observation. Against this background, in the blood of patients, a stable normalization of plasma lipid activity was noted at the same time - after 4 months. the content of AGP in it was 1.66 ± 0.005 D_{233} / 1 ml, TBA-active products - 3.41±0.002 μmol / l with optimization of the antioxidant potential of the liquid part of the blood (36.3±0.05%).

The imbalance of metabolites of arachidonic acid, thromboxane B2, was increased by 84.8%, whereas the level of the derivative of its functional antagonist, 6-keto-prostaglandin F1α, was reduced by 17.9% (Table 2). 1). This was accompanied in the patients with high level of endothelin-1 (21.1±0.27 pg/ml) with a decrease in the amount of total metabolites of nitric oxide by 28.7% in their blood plasma.

The complex therapy was accompanied in patients by gradual normalization of arachidonic acid metabolites in their blood - a decrease in thromboxane B2 by 85.5%, and an increase in 6-keto-prostaglandin F1α by 14.3% (Table 1). This was accompanied by a decrease in the plasma of the examined patients to the level of control of endothelin-1 (8.1±0.22 pg/ml) and an increase in the amount of total metabolites of nitric oxide (by 21.9%).

At the end, platelet aggregation in patients with AH of grade 3 in MS was enhanced (Table 2). Most actively, their platelets reacted to collagen, while the degree of aggregation with this inductor exceeded the control by 25.0%, and the aggregation rate by 27.5%. Slightly less platelets of patients responded by aggregation to ristomycin. At the same time, the degree of aggregation with it in patients was above the control by 25.7%, and the aggregation index exceeded it in healthy individuals by 46.4%. Even less active platelets of the examined patients aggregated in response to the addition of ADP. In this case, the value of

ADP aggregation and the aggregation index with this inducer exceeded the control values by 25.7% and 58.4%, respectively.

Against the background of temporary venous occlusion in the outcome, platelet aggregation in the observed patients was strengthened (Table 2). The most active platelets in plasma taken with cuff application reacted to collagen, while the degree of aggregation with this inductor exceeded the control by 46.3%, and the aggregation index by 50.0%. Slightly less platelets of patients responded with aggregation to ristomycin: the degree of aggregation with it in patients in a sample with temporary venous occlusion was higher than control by 52.1%, and the aggregation index exceeded that in healthy individuals by 85.7%. Even less active platelets of the examined patients in plasma after occlusive action were aggregated in response to the addition of ADP. In this case, the value of ADP aggregation and the aggregation index with this inducer in these conditions exceeded the control values by 63.8% and 81.2%, respectively.

In the outcome of ISTAT and IPAT in observed individuals with AH of grade 3, MS was significantly decreased: with collagen by 14.8% and 14.0%, respectively, with ristomycin by 16.2% and 14.5%, respectively, with ADP by 19.9% and 18.4%, respectively (Table 2).

As a result of the use of complex therapy in observed patients, platelet aggregation experienced a gradual weakening, maximally expressed by 4 months. observations, which allowed it to reach the level of control (Table 2). Thus, during these periods of treatment, the normalization of collagen aggregation was noted, manifested by a decrease in the degree of aggregation of platelets with this inducer by 26.2% and a decrease in the aggregation index by 28.9%. The achieved normalization of the aggregation response of platelets of patients in these terms to ristomycin was provided by a decrease in the degree of aggregation with it by 28.8% with a decrease in the aggregation index by 57.4%. Regarding the third tested inductor - ADP platelets examined patients after 4 months. Therapies reacted with aggregation to the same extent as in the control. This was due to a decrease in the degree of ADP aggregation and the aggregation rate with this agonist by 29.2% and 45.6%, respectively.

In a sample with temporal venous occlusion in patients undergoing complex treatment, platelet aggregation also gradually weakened, reaching a control level by 4 months. observations (Table 2). Thus, in the plasma obtained against the background of temporary venous occlusion, during these periods of treatment the normalization of collagen aggregation was noted due to a decrease in the degree of aggregation of platelets with this inducer by 46.2% with a decrease in the aggregation index with collagen by 50.0%. The achieved normalization of platelet aggregation response in patients with temporal venous occlusion at this time on ristomycin was provided by a decrease in the degree of aggregation with it by 52.1% with a decrease in the aggregation index by 80.5%. Regarding the third tested inductor, ADP, platelets in the plasma obtained after the application of the mantle in the patients examined after 4 months. therapies responded with aggregation to the same extent as in control by decreasing aggregation and aggregation rates with this agonist by 60.4% and 81.1%, respectively.

After 4 months. of complex therapy in the observed patients, the values of ISTAT and IPAT in all cases reached the level of control due to their increase for collagen by 14.2% and 14.0%, for ADP by 19.3% and 17.3%, for ristomycin by 15, 7% and 13.9%, respectively. Continuation of therapy ensured the preservation of the normal level of AT and vascular control of it until the end of observation.

When studying intravascular activity of platelets (Table 2) in patients with AH of the third degree in MS, a decrease in the number of discocytes to 48.6 ± 0.40% (in control - 82.1 ± 0.10%) was revealed. The content of disco-echinocytes in their blood was doubled. The number of spherocytes, sphero-echinocytes and bipolar platelet forms also significantly exceeded the control values and reached 14.4±0.08%, 7.0±0.06% and 2.2±0.07%, respectively, in patients. The sum of active forms of platelets in patients was 51.4±0.12%, (in control - 17.9±0.09%). Small and large aggregates in the blood of the subjects of the observation group contained 18.6 ± 0.08 and 5.4 ± 0.04, against control - 2.9±0.06 and 0.2±0.06 per 100 free-standing platelets, respectively. The number of platelets in the aggregates in patients exceeded the level of the comparison group by 2.2 times, which indicated a marked increase in their intravascular activity of platelets.

When assessing intravascular activity of platelets in conditions of temporary venous occlusion (Table 2) in patients with AH of grade 3, a reduced number of discocytes was found in MS with 63.2±0.50% (in control

- 94.3±0.12%). At the same time, the content of disco-echinocytes in their blood was increased almost 9-fold. The number of spherocytes, sphero-echinocytes and bipolar platelet forms in plasma obtained after application to the cuff was also significantly higher than the control values and reached 12.3±0.05%, 4.2±0.05% and 1.6±0,02%, respectively, accompanied by a high value of the sum of active forms of platelets. At the same time, against the background of temporary venous occlusion of small and large aggregates in the blood of the subjects of the observation group, 16.7±0.05 and 4.2±0.04 were kept, against control - 1.8±0.50 and 0.02±0.004 per 100 free-standing platelets, respectively, with a 2.4-fold increase in the number of platelets in the aggregates compared to the level of the control group.

The complex therapy provided the patients with rapid weakening of intravascular activity of platelets, which allowed, after 4 months. to achieve normalization of the level of discocytes (80.7±0.20%). At the same time, the number of disco-echinocytes in their blood decreased twice, and initially increased number of spherocytes, sphero-echinocytes and bipolar forms of platelets after 4 months. The monitoring also reached the indicators characteristic of control. This ensured that under these conditions the total number of active platelet forms decreased to the control level (19.3 ± 0.03%). Also in the blood of individuals of the observation group to 4 months. the number of small and large aggregates corresponded to the control level (13.1±0.02 and 0.28±0.004 per 100 free-standing platelets, respectively) with the normalization of the platelet count in them. Further complex therapy provided stable preservation of normal intravascular activity of platelets in all patients until the end of observation.

In addition, the complex therapeutic effect was carried out in the patients who underwent rapid normalization of vascular control of intravascular platelet activity, which, after 4 months, increase the level of discocytes against the background of temporary venous occlusion to control values (93.1 ± 0.50%). At the same time, the number of disco-echinocytes, spherocytes, sphero-echinocytes and bipolar forms of platelets in the blood taken at the time of application of the cuff, after 4 months. observations significantly decreased, also reaching the indicators inherent in control. In these terms, a reduction in the cuff sample to the level of the control group of the total number of active platelet forms (6.9 ± 0.04%) was ensured during these periods. In the blood of the individuals of the observation group obtained upon application to the vessel of the cuff, by 4 months. the number of small and large aggregates also reached the control level (2.0 ± 0.005 and 0.03 ± 0.001 per 100 free-standing platelets, respectively) with the normalization of the number of platelets included in them. Further complex therapy provided a complete and stable control of the vascular wall over the intravascular activity of platelets.

DISCUSSION

In previous studies, it was found that MS, especially in combination with complicated AH, actively violate the functions of the vascular wall and platelets, thereby promoting the occurrence of repeated thrombotic episodes [20]. At the same time, the activity of platelet hemostasis in these patients is still not fully understood, and needs additional evaluation [21]. At the same time, this category of patients does not fully explain the degree of violation of the main mechanisms of formation of thrombocytopathy, as the basis of thrombophilia [22,23].

At the time of taking under observation in blood, an increase in lipid concentration was found in all patients, which threatened rapid progression in this category of atherosclerosis patients. At the basis of the formation of atherogenic danger, an increase in LPO in the blood also played a major role, causing not only peroxide changes in plasma lipids, but also damage to endotheliocytes, which facilitated the penetration of lipids into the vessel wall, thereby reducing its antiaggregant properties [24].

The observed increased BP had a negative effect on the vascular wall itself, causing damage to the endothelium and exposing subendothelial fibers that are able to contact platelets activly [25,26]. In the emerging conditions in the vascular wall, the synthesis of biologically active substances, which were able to limit the adhesion and aggregation of platelets, in which the synthesis of proaggregants was increased [27], was lowered. Thus, the intensification of thromboxane formation and the weakening of the production of its functional prostacyclin antagonist, observed in the observed patients, created an imbalance of arachidonic acid metabolites, apparently based on the activation of platelet thromboxane synthetase and depression of vascular prostacyclinsynthetic activity [28]. These disorders were exacerbated by the developing increase in production in the wall of the vessels of edothelin-1 and the weakening of the production of NO in it, probably

as a result of suppression of endothelial NO synthase by excessive LPO and dyslipidemic changes in plasma [29].

Developing with AH and MS biochemical disorders in the blood plasma were inevitably accompanied by an increase in AT, which was noted for all tested inducers. Excessively formed on their membranes, plasma thromboplastin, stimulated thrombin formation, leading to the growth of aggregates of the blood platelets and the acceleration of the formation of fibrin fibers on them with the formation of platelet-fibrin clots capable of embolizing small vessels [30].

The initially high sensitivity of platelets to the aggregation inducers found in the examined patients was provided through the activation of a number of mechanisms. Thus, on the surface of platelets, a significant increase in the density of glycoproteins Ia-IIa and VI, participating in the adhesion of blood platelets, occurred at the surface of platelets at the time of enrollment, as could be judged by the intensification of AT in response to collagen [31]. This was inevitably accompanied by activation of phospholipase C, stimulation of the synthesis of diacylglycerol and protein kinase C, followed by pronounced phosphorylation of the proteins of the contractile system. Under these conditions, inositol triphosphate actively stimulated the entry of Ca2 + from the depot of the blood plates, contributing to the rapid reduction of actomyosin [32].

Intensification of adhesion of blood platelets in the observed patients is also associated with excessive expression of receptors to the Willebrand factor on their surface. This mechanism of enhancing the adhesive activity of platelets in patients was documented by the intensification of AT with ristomycin affecting platelets, identical to the subendothelial structures of the vessels. In this case, in view of the fact that for the onset of ristomycin AT, the von Willebrand factor is required that fixes one side of the molecule to ristomycin (as to collagen) and the second to the blood plates through their receptor - Ic, in this category of patients it can be ascertained that the formation of the "adhesion axis »: Ristomycin (collagen) - von Willebrand factor - GPIv. In this case, it is the significant increase in the number of binding sites of von Willebrand factor on the membranes of the blood platelets of the observed patient category is an important mechanism for the onset of excessive adhesive capacity of thrombocytes [33].

The ADP agonist, referring to the weak inducers of platelet aggregation, under conditions of a lack of formation in the vessels of nitric oxide and prostacyclin also actively interacted with its own receptors on the membranes of the blood platelets. This caused on them a powerful expression of fibrinogen receptors with activation of phospholipase A2, which provides the cleavage of arachidonic acid from membrane phospholipids [34].

The complex correction provided stable elimination of dyslipidemia within 4 months. therapy, which, combined with an increase in antioxidant plasma protection and a decrease in the concentration of primary and secondary LPO products, minimized the risk of progression in observed patients of atherosclerosis [35,36,37].

Excess blood of patients with active forms of blood platelets was based, on the one hand, on the lack of formation of nitric oxide and prostacyclin in the vascular walls, and, on the other, increased activity of the platelets themselves. In addition, the high intravascular activity of platelets spoke of the excessive availability of blood vessel collagen for the vascular wall due to damage to its endothelium on the background of a constant presence in the blood of patients of increased concentrations of dissolved aggregation inducers, a large amount of lipids and active LPO leading to chemical damage to the endothelium [6]. Developing increase in the content of active forms of platelets contributed to an increase in blood-moving aggregates of different sizes, capable of damaging endotheliocytes, which additionally caused exposure of subendothelial structures. These processes close the "vicious circle", causing a significant weakening of vascular hemostasis and an increased risk of thrombosis [3].

The normalization of blood pressure achieved on the background of treatment quickly eliminated the negative effect of hemodynamic disturbances on the vascular wall peculiar to hypertension, minimizing the alteration of the endothelium and the expression of subendothelial fibers capable of activating platelets [7]. Early relief of hypercholesterolemia also significantly weakened vasopathy [11], activating in the vessel wall the synthesis of biologically active substances inhibiting adhesion and aggregation of platelets while physiological weakening of the synthesis of proaggregants in them. This manifested itself in patients after 4

months. recovery against the background of complex therapy to the level of control of the balance of thromboxane and prostacyclin, as judged by the dynamics of the concentration of their metabolites. Fast-advancing positive changes were combined with suppression to the control level of production in the wall of the vessels of edothelin-1 and increased production of NO in it, probably as a result of activation of endothelial NO synthase against the background of normalization of LPO and plasma lipid composition [13].

The performed therapy was able not only to increase the production of NO and prostacyclin in the vessels, but also to lower the sensitivity of platelets to the inducers of their aggregation. So, on their surface in treated patients after 4 months. observations developed, judging by the weakening of AP in response to collagen, a significant decrease in the density of glycoproteins Ia-IIa and VI, involved in the adhesion of blood platelets. The found normalization of adhesion of the blood platelets against the background of therapy in the observed patients was also weakened by reducing the number of receptors to the von Willebrand factor on them, as indicated by inhibition to the level of control of AT with ristomycin [21].

The use of complex therapy provided on the surface of platelets in patients with AH of grade 3 with MS a decrease in the number of sites of fixation of a strong inducer of collagen. This was based on a decrease in the activity of phospholipase C, a decrease in the synthesis of diacylglycerol and protein kinase C with inhibition, phosphorylation of proteins in the contractile system of platelets. The decrease in the amount of inositol triphosphate provided a slowing down of the intake of Ca^{2+} from the depot of the blood platelets, contributing to a decrease in the reduction of actomyosin [8, 22].

At the same time by 4 months. the observed inhibition of AP with ADP indicated a physiological analysis of the expression of fibrinogen receptors on platelets and the activity of phospholipase A2 in them, which provided the cleavage of only the optimal amounts of arachidonic acid from the membrane phospholipids of the blood platelets [5].

Complex therapy caused a rapid reduction in the blood of patients in the number of active forms of blood platelets, which was based, on the one hand, on the increase in the formation of nitric oxide and prostacyclin in the vascular walls, and on the other, the weakening of the activity of the platelets themselves. At the same time, inhibition of intravascular activity of platelets against the background of the treatment indicated that the availability of collagen for the vascular wall for blood plates was minimized due to the minimization of chemical damage to its endothelium by a drop in the amount of dissolved aggregation inducers, lipids and lipid peroxidation products in the blood of patients [2]. The reduction in the active platelet form in these conditions was accompanied by the normalization of the number of aggregates of different sizes moving across the blood, which also played a role in normalizing mechanical effects on endotheliocytes, minimizing the contact of subendothelial structures with blood. Effects due to treatment were able to break this "vicious circle", providing a significant increase in vascular control over platelet activity, significantly lowering the risk of thrombosis.

CONCLUSION

The surplus platelet activity observed in the in vitro and in vivo patients is based on an increase in their adhesive and aggregation activity due to the imbalance of pro- and antiaggregation effects occurring in their blood. The most significant causative factors in this situation should be considered arterial hypertension, negative changes in the lipid composition of plasma and the enhancement of LPO in it. Carrying out the therapy, including amlodipine, valsartan, pioglitazone, hypocaloric diet and physical doses, after 4 months. provides in patients with hypertension of grade 3 with MS stable normalization of initially high platelet activity and reduced vascular control over it despite the subsequent non-strict observance of the non-medicamentous component of the complex effect.

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Table 1. Dynamics of biochemical characteristics of plasma in patients with complicated arterial hypertension of the 3rd degree with metabolic syndrome in the context of complex therapy

options	Dynamics of the considered indicators, n = 24, M ± m					Control, n = 25, M ± m
	initial state	2 months	4 months	12 months	36 months	
Concentration of total cholesterol, mmol / l	6.25±0.07**	5.79±0.06**	4.83±0.06	4.88±0.03	5.18±0.04	4.79±0.02
Concentration HDL cholesterol, mmol / l	1.14±0.003**	1.31±0.001**	1.50±0.002	1.51±0.006	1.43±0.01	1.53±0.001
Concentration of LDL cholesterol, mmol / l	3.92±0.06**	3.42±0.05**	2.60±0.08	2.62±0.04	2.87±0.03	2.56±0.03
Concentration Cholesterol VLDL, mmol / l	1.19±0.002**	1.06±0.003**	0.73±0.003	0.72±0.008	0.71±0.002	0.70±0.002
Concentration triglycerides, mmol / l	2.63±0.02**	2.34±0.008**	1.61±0.006*	1.65±0.01*	1.93±0.02*	1.56±0.01
Level of total lipids, g/l	8.79±0.03**	7.53±0.04**	5.29±0.02	5.34±0.03	5.92±0.04	5.26±0.04
Concentration acylhydroperoxides plasma, D_{233}/1 ml	3.62±0.03**	3.24±0.02**	1.66±0.005	1.65±0.006	1.69±0.002	1.62±0.02
Thiobarbituric acid-products of plasma, µmol / l	5.76±0.002**	5.32±0.003**	3.41±0.002	3.44±0.002	3.86±0.004	3.38±0.006
Antioxidant activity of plasma, %	21.4±0.06**	26.6±0.40**	36.3±0.05	36.7±0.12	34.4±0.50	36.8±0.03
Thromboxane B_2, pg / ml	291.4±0.68**	212.6±0.54**	157.1±0.42	156.7±0.36	157.0±0.46	156.5±0.66
6-keto-prostaglandin F1α, pg / ml	70.2±0.42**	74.9±0.35**	81.9±0.46	82.3±0.29	82.2±0.38	82.4±0.49
Total metabolites of nitric oxide, µmol / l	26.3±0.52**	29.6±0.45**	33.7±0.40	33.9±0.48	33.7±0.37	33.6±0.35
Endothelin-1, pg / ml	20.9±0.26**	12.8±0.19**	8.1±0.22	8.2±0.16	8.2±0.14	8.2±0.15

Legend of the reliability of the differences between the group of patients and control: * - p <0.05; ** - p <0.01. In the following tables, the notation is similar.

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Table 2. Aggregational activity of thrombocytes in patients with complicated arterial hypertension of the 3rd degree in the metabolic syndrome with a complex correction

options	Dynamics of the considered indicators, n = 24, M ± m					Control, n = 25, M ± m
	initial state	2 months	4 months	12 months	36 months	
Aggregation of platelets with collagen:						
degree of aggregation, relative units	10.1±0.25**	9.4±0.32**	8.0±0.27	8.1±0.25	7.9±0.29	8.0±0.32
degree of aggregation against a background of venous occlusion, relative units	7.9±0.35**	6.8±0.32**	5.4±0.25	5.4±0.28	5.3±0.26	5.4±0.29
index of the degree of platelet ggregation	1.27±0.11**	1.38±0.09**	1.48±0.12	1.49±0.08	1.49±0.07	1.49±0.09
ag aggregation index against venous occlusion, relative unitsgregation rate, relative units	8.9±0.32**	7.8±0.36**	6.9±0.40	6.8±0.24	6.9±0.20	6.9±0.27
aggregation index against venous occlusion, relative units	6.9±0.31**	5.6±0.24**	4.6±0.25	4.5±0.21	4.6±0.24	4.6±0.25
platelet aggregation index	1.29±0.12**	1.39±0.09**	1.50±0.14	1.50±0.17	1.50±0.09	1.50±0.13
Aggregation of platelets with ADP:						
degree of aggregation, relative units	9.3±0.34**	8.3±0.30**	7.2±0.22	7.1±0.25	7.0±0.27	7.1±0.24
degree of aggregation against a background of venous occlusion, relative units	7.7±0.37**	6.2±0.29**	4.8±0.31	4.7±0.27	4.7±0.24	4.7±0.26
index of the degree of platelet aggregation	1.21±0.13**	1.34±0.11**	1.50±0.12	1.51±0.08	1.50±0.06	1.51±0.07
aggregation rate, relative units	8.3±0.29**	7.2±0.27**	5.7±0.23	5.6±0.15	5.5±0.22	5.6±0.16
aggregation index against venous occlusion, relative units	6.7±0.28**	5.2±0.24**	3.7±0.27	3.7±0.22	3.6±0.24	3.7±0.23
platelet aggregation index	1.24±0.12**	1.38±0.14**	1.52±0.09	1.51±0.08	1.51±0.10	1.52±0.09
Aggregation of platelets with ristomycin:						
degree of aggregation, relative units	9.4±0.22**	8.5±0.29**	7.3±0.28	7.4±0.18	7.3±0.23	7.4±0.19
degree of aggregation against a background of venous occlusion,						

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relative units	7.3±0.26**	6.0±0.23**	4.8±0.20	4.8±0.25	4.8±0.18	4.8±0.21
index of the degree of platelet aggregation	1.29±0.14**	1.41±0.09**	1.53±0.08	1.54±0.10	1.53±0.11	1.54±0.10
aggregation rate, relative units	8.5±0.30**	7.2±0.26**	5.4±0.22	5.3±0.26	5.2±0.19	5.3±0.22
aggregation index against venous occlusion, relative units	6.5±0.30**	5.1±0.27**	3.6±0.23	3.5±0.25	3.4±0.26	3.5±0.26
platelet aggregation index	1.30±0.13**	1.42±0.10**	1.51±0.12	1.52±0.08	1.52±0.07	1.52±0.06

Table 3. Intravascular activity of thrombocytes in patients with complicated arterial hypertension of the third degree in the metabolic syndrome with a complex correction

options	**Dynamics of the considered indicators, n = 24, M ± m**					**Control, n = 25, M ± m**
	initial state	2 months	4 months	12 months	36 months	
Discolets, %	49.4±0.20**	59.5±0.40**	80.7±0.20	79.8±0.40	77.5±0.70	82.1±0.10
Number of discs during venous occlusion, %	63.2±0.50**	69.8±0.23**	93.1±0.50	92.6±0.20	91.2±0.40	94.3±0.12
Disco-echinocytes, %	27.3±0.09**	23.8±0.15**	13.8±0.09	14.3±0.05	15.6±0.09	13.5±0.04
Number of disco-echinocytes during venous occlusion, %	18.7±0.06**	14.5±0.08**	2.5±0.05	2.7±0.03	3.1±0.02	2.12±0.18
Spherocytes, %	14.5±0.08**	10.9±0.08**	2.7±0.04	2.6±0.03	3.2±0.04	2.1 ±0.12
Number of spherocytes during venous occlusion, %	12.3±0.05**	11.1±0.07**	2.0±0.02	2.2±0.02	2.8±0.03	1.6±0.04
Sphero-echinocytes, %	6.7±0.01**	4.2±0.07**	1.8±0.01	2.1±0.02	2.3±0.04	1.5±0.08
Number of sphero-echinocytes during venous occlusion, %	4.2±0.05**	3.4±0.02**	1.6±0.006	1.7±0.02	1.9±0.01	1.3±0.06
Bipolar forms, %	2.1±0.004**	1.6±0.01**	1.0±0.002	1.2±0.01	1.4±0.02	0.8±0.04
Number of bipolar forms during venous occlusion, %	1.6±0.002**	1.2±0.006**	0.8±0.005	0.8±0.005	1.0±0.004	0.7±0.08
Sum of active forms, %	50.6±0.15**	40.5±0.05**	19.3±0.03	20.2±0.10	22.5±0.30	17.9±0.09
The amount of the sum of active forms during venous occlusion, %	36.8±0.30**	30.2±0.30**	6.9±0.04	7.4±0.06	8.8±0.04	5.7±0.90
The number of platelets in the aggregates, %	15.5±0.04**	12.5±0.07**	6.9±0.03	7.1±0.04	7.8±0.03	6.7±0.08
The number of platelets in the aggregates during venous occlusion, %	11.7±0.02**	9.8±0.05**	5.1±0.02	5.5±0.03	5.7±0.04	4.9±0.15
The number of small aggregates of 2-3						

thrombocytes per 100 free-standing platelets	18.2±0.09**	14.4±0.04**	3.1±0.02	3.3±0.02	3.7±0.05	2.9±0.06
The basal number of small aggregates of 2-3 platelets per 100 free platelets during venous occlusion, %	16.7±0.05**	13.1±0.08**	2.0±0.005	1.9±0.01	2.3±0.02	1.8±0.05
The number of medium and large aggregates, 4 or more platelets per 100 free-standing platelets	5.7±0.03**	2.5±0.01**	0.28±0.004	0.25±0.002	0.29±0.003	0.2±0.06
The number of medium and large platelet aggregates of 4 or more cells per 100 free platelets during venous occlusion, %	4.2±0.04**	3.2±0.03**	0.03±0.001	0.04±0.004	0.04±0.002	0.02±0.004

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