

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Physiological Reaction of The Ability of Erythrocytes to Aggregate to Cessation of Prolonged Hypodynamia.

Vorobyeva NV^{1*}, Skripleva EV¹, Makurina ON², and Mal GS³.

¹South-West state University, Kursk, Russia.

²Samara National Research University, Samara, Russia.

³Kursk state medical university, Kursk, Russia.

ABSTRACT

Aggregation of erythrocytes mostly determines the processes of microcirculation and metabolism in tissues. Studying of their peculiarities in untrained people who began regular adequate exercises, can help to understand rehabilitation mechanisms after hypodynamia. To estimate the dynamics of erythrocytes' aggregation in persons of the second mature age who avoided physical loads earlier and began regular exercises. The group of observation was composed of 45 healthy people of both sexes of the second mature age who avoided physical loads earlier and began regular exercises in the athletic section thrice a week. The 1st control group was composed of 42 people of both sexes of the same age who had regularly trained in the athletics section thrice a week for not less than 10 years. The 2nd control group was composed of 46 people who had daily walked not less than 6 km in the course of the last 10 years. There were applied biochemical, hematological and statistical methods of investigation. The start of regular exercises in persons with hypodynamia was accompanied by quantity lowering of acylhydroperoxides in their plasma in 3 months of observation by 14.8%, and in 6 months – by 23.4% reaching the level of both control groups. It took place against the background of strengthening of their antioxidant plasma activity in 6 months by 10.2%. During 6 months of physical trainings the group of observation was noted to have imbalance decrease of arachidonic acid metabolites: the level of thromboxane B₂ in their plasma lowered by 10.7% and the level of 6-keto-prostaglandin F_{1α} rose by 8.7%. It was accompanied by summary increase of nitric oxide metabolites by 8.9% in their plasma. In 6 months the group they were found to have the lowering of erythrocytes' involvement into aggregates by 17.3% and the quantity of these aggregates by 39.3% at the increase of free erythrocytes by 13.5%. For people of second adulthood who started regular physical activity after prolonged hypodynamia, the gradual weakening of erythrocyte aggregation attains the level of control groups.

Keywords: the second mature age, prolonged hypodynamia, erythrocytes, aggregation, athletic loads.

**Corresponding author*

INTRODUCTION

Low physical activity is rather widespread among modern people [1, 2]. It causes realization of many variants of hereditary predisposition to pathology [3, 4]. It was traced in different categories of population of industrially developed countries [5, 6] and confirmed in experiment [7, 8, and 9]. Evident consequences of hypodynamia in a man can manifest themselves already in young age increasing the frequency of episodes of temporary disability because of weakening of functional reserves of the whole body [10, 11]. While aging low physical activity leads to aggravation of many diseases and their chronic course [12, 13]. Lasting hypodynamia worsens many blood indices [14, 15]. It is connected with the fact that low muscle activity causes the development of some functionally unfavorable changes in a body [16]. As previous researches showed, low physical activity was accompanied by micro rheological dysfunctions of some regular blood elements already in young age what promoted the start of hypoxia formation in tissues [17, 18]. Developing in these conditions chronic oxygen deficiency worsened the course of anabolic processes in the whole body and weakened its common vitality [19, 20]. All this formed the basis for pathology development in the internals [21, 22] and promoted the appearance of steady vessels' spasm [23, 24]. It was tracked that conditions for arterial pressure rise could be often formed against the background of hypodynamia what led to gradual development of arterial hypertension [25, 26]. Besides, hypodynamia aggravated the course of already existing cardio-vascular pathology and promoted the formation of resistance to the applied pharmacological therapy [27, 28] in these patients. Taking into account the evidence of hypodynamia negative impacts on a body, the search of a way out of the given state which can improve erythrocytes' aggregation, becomes really urgent. In this respect it seems to be important to estimate the impact of exercises (as the most available and safe physical loads) on erythrocytes' aggregation in persons of the second mature age who avoided regular physical loads within lifetime. The following aim was put in this research: to estimate the dynamics of erythrocytes' aggregation in persons of the second mature age who avoided physical loads earlier and began regular exercises.

MATERIALS AND METHODS

The conduction of the research was approved by the local Ethics Committee of the South-West state University in May, 25th, 2016 (Record №5). All the examined persons gave written informed consent on participation in the conducted research. The study was conducted on people living in town Kursk and Kursk region. The group of observation was composed of 45 people of both sexes (23 men and 22 women) of the first mature age (mean age 44.9 ± 2.2 years) who had purposefully avoided regular physical exercises during lifetime. They started regular trainings in the athletic section thrice a week at the duration of not less than an hour. The 1st group of control was composed of 42 healthy people of both sexes (22 men and 20 women) of the second mature age (mean age – 42.8 ± 2.6 years) who regularly trained for not less than 10 years in the athletic section thrice a week at the duration of each training of not less than an hour. The first control group was composed of 42 healthy people of both sexes (22 men and 20 women) of the second mature age (mean age 42.8 ± 2.6 years) who had regularly trained in athletics section thrice a week for not less than 10 years at duration of each training for not less than an hour. The second control group was composed of 46 people of the second mature age (mean age 43.7 ± 2.3 years) who had tried to walk daily the distance of 5 km and had had no additional exercises. Existing in some persons from the group of observation and the control groups chronic diseases (chronic bronchitis, chronic tonsillitis, and chroniccholecystitis) had been in the state of stable remission for not less than 2 years. All the enrolled into the research persons were once observed and examined.

The activity of the processes of lipids' peroxidation (LPO) in blood plasma was determined according to the content of Thiobarbituric acid (TBA)-active products in it by a kit of the firm "Agat-Med" (Russia) and according to the level of acylhydroperoxides (AHP). Antioxidant plasma activity was registered [29]. The content of thromboxane B₂ and 6-keto-prostaglandin F_{1 α} in plasma of the examined persons was determined with the help of immune-enzymatic analysis by a kit of the firm "Ensor Life science" (USA). Summary content of nitric oxide metabolites was also determined in plasma [30].

Erythrocytes' capacity to spontaneous aggregation was established with the help of light microscopy by calculating the quantity of erythrocytes' aggregates, the number of aggregated and non-aggregated erythrocytes [31] in Gergiev's box.

In the group of observation the persons were examined at the beginning and in 3 and 6 months of trainings. All the persons from both control groups were observed and examined once.

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

RESULTS AND DISCUSSION

Persons from the group of observation were noted to have strengthening of LPO processes (Table). The quantity of AHP and TBA-products in their plasma surpassed the values in the 1st control group by 40.6% and 33.0%, in the 2nd control group – by 38.1% and 30.9%, respectively. It took place against the background of weakening of plasma antioxidant activity in them in comparison with the 1st control group by 18.5%, in comparison with the 2nd control group – by 16.9%.

Table: Hematologic parameters in people who started regular physical activity after prolonged low physical activity

Indicators	Persons who started physical training after prolonged hypodynamia, n=45, M±m			Control1, n=42, M±m	Control 2, n=46, M±m
	initial state	3 months	6 months		
Acylhydroperoxides of plasma, D ₂₃₃ /l ml	2.32±0.57 p<0.01 p ₁ <0.01	2.02±0.64 p<0.01 p ₁ <0.01	1.88±0.49 p<0.05 p ₁ <0.05	1.65±0.20	1.68±0.17
Thiobarbituric acid-products of plasma, mkmol/l	4.19±0.59 p<0.01 p ₁ <0.01	3.75±0.32 p<0.01 p ₁ <0.01	3.41±0.20 p<0.05 p ₁ <0.05	3.15±0.23	3.20±0.26
Antioxidant activity of plasma, %	26.5±0.48 p<0.01 p ₁ <0.01	27.8±0.43 p<0.01 p ₁ <0.01	29.2±0.47 p<0.05 p ₁ <0.05	31.4±0.46	31.0±0.37
thromboxan B ₂ , pg / ml	208.5±0.72 p<0.01 p ₁ <0.01	197.4±0.69 p<0.01 p ₁ <0.01	188.4±0.61 p<0.05 p ₁ <0.05	162.2±0.72	165.1±0.68
6-keto-prostaglandin F _{1α} , pg / ml	83.0±0.35 p<0.01 p ₁ <0.01	86.4±0.39 p<0.05 p ₁ <0.05	90.2±0.42 p<0.05 p ₁ <0.05	95.0±0.45	94.3±0.54
nitric oxide's metabolites, umol/l	31.2±0.28 p<0.01 p ₁ <0.01	32.7±0.22 p<0.01 p ₁ <0.01	34.0±0.25 p<0.05 p ₁ <0.05	37.2±0.32	35.8±0.32
sum of all the erythrocytes in an aggregate	40.7±0.14 p<0.01 p ₁ <0.01	37.2±0.16 p<0.01 p ₁ <0.01	34.7±0.18	31.5±0.10	32.1±0.07
quantity of aggregates	8.2±0.09 p<0.01 p ₁ <0.01	7.5±0.07 p<0.01 p ₁ <0.01	7.0±0.06	6.0±0.07	6.2±0.09
quantity of free erythrocytes	245.0±0.45 p<0.01 p ₁ <0.01	262.8±0.52 p<0.05 p ₁ <0.05	278.1±0.49	296.1±0.35	292.3±0.29

Conventions: p – the significance of differences in the parameters of those surveyed who have inactivity and control 1 group;

p₁ – the significance of differences in the parameters of those surveyed who have inactivity and control 2 groups; the significance of differences between indicators 1 and 2 are not detected.

Blood of the examined persons with hypodynamia in the initial state was noted to have imbalance of

arachidonic acid metabolites: the level of thromboxane B₂ in their plasma turned out to be higher in comparison with the 1st control group by 28.5%, in comparison with the 2nd control group – by 26.3%. The level of 6-keto-prostaglandin F_{1α} in the group of observation at that was lower in comparison with the 1st control group by 14.4%, in comparison with the 2nd control group – by 13.6% (Table). It was accompanied in them by content lowering of the quantity of nitric oxide summary metabolites in plasma (by 19.2% in comparison with the 1st control group and by 14.7% in comparison with the 2nd control group).

At the same time, in the initial state the examined persons with hypodynamia were found to have strengthening of erythrocytes' aggregative properties. It was pointed at by the index increase of summary erythrocytes' involvement into aggregate by 29.2% and 26.8% (in comparison with the level of the 1st and the 2nd control groups) and quantity increase of these aggregates by 36.7% and 32.2% at decrease of freely lying erythrocytes by 20.8% and 19.3%, respectively.

The start of regular athletic loads was accompanied by positive dynamics of accountable indices. The group of observation was noted to have weakening of LPO processes against the background of physical loads (Table). The quantity of AHP and TBA-products in plasma of persons from the group of observation lowered in 3 months of observation by 14.8% and 11.7%, and in 6 months – by 23.4% and 22.9% in comparison with the beginning. However, the level of both control groups wasn't reached. It took place against the background of strengthening of plasma antioxidant activity in them in 3 months by 4.9%, in 6 months – by 10.2% thus approaching the control levels.

The blood of persons with hypodynamia who began physical trainings was noted to have the lowering of imbalance evidence of arachidonic acid metabolites: the level of thromboxane B₂ in their plasma lowered in 3 months of observation by 5.6%, in 6 months – by 10.7%. At that, the level of the derivative of its functional antagonist – 6-keto-prostaglandin F_{1α} in the group of observation rose in 3 months by 4.1% in comparison with the beginning, in 6 months – by 8.7% (Table). It was accompanied in them by content rise of the quantity of nitric oxide summary metabolites in plasma (by 4.8% - by the 3rd month of trainings and by 8.9% - by the 6th month of trainings).

At the same time, those persons who had hypodynamia earlier, were found to have weakening of erythrocytes' aggregative properties against the background of athletic loads. It was pointed at by the lowering of erythrocytes' summary involvement into aggregates in 3 and 6 months by 9.4% and 17.3%, and the quantity of these aggregates by 39.3% and 17.1% at the increase of freely lying erythrocytes by 7.3% and 13.5%, respectively.

Lasting maintenance of physiological optimum in a human body and its effective rehabilitation are possible only at high muscle activity [32]. It was noted long ago that hypodynamia could cause prepathological state and strengthen existing pathology [33, 34]. Last decades notwithstanding the successes of medicine and propaganda of medical knowledge hypodynamia remains rather widespread among population of developed countries. Its consequences at that continue to damage economically because of high frequency of working capacity lowering [35] against its background. It's noted that formation of hypodynamia is accompanied by not only worsening of musculoskeletal system state but also lowering of metabolism intensity. Given situation negatively influences the functioning of the whole body [36].

There is some basis to suspect that great significance in the formation of hypodynamia consequences belongs to disturbances of regular blood elements' micro rheological properties and, first of all, to their most numerous population – erythrocytes [37, 38]. At the same time, the weakening of antioxidant defense of the organism, leading to an increase in plasma and LPO intensity, is of particular importance for their development. Excess of lipid peroxidation products in plasma causes membrane rearrangements of these cells from the outside and from the inside, which worsens their functions [32].

Found strengthening of erythrocytes' aggregation at hypodynamia can be estimated as the result of the combined impact of low physical activity's consequences on micro rheological processes. A significant increase in plasma lipid peroxidation inevitably leads to an increase in the blood of these people the number of erythrocyte aggregates and an increase in the degree of involvement in them of all new erythrocytes. Found evidence increase of erythrocytes' aggregation in conditions of hypodynamia can be mostly explained by strengthening impact of catecholamines on them. Their level reliably rises in blood at any dysfunction [40].

Quantity increase of catecholamines in blood of persons from the group of observation should be mostly estimated as the mechanism of metabolism intensification in tissues [41, 42].

The synthesis of biologically active substances which can limit erythrocytes' aggregation lowers in vascular wall of persons with hypodynamia. At the same time, the level of pro-aggregates rises in their blood. So, noted in group of observation intensification of thromboxane formation and production weakening of its functional antagonist – prostacyclin – forms imbalance of arachidonic acid metabolites. Given disturbances are aggravated in them by developing weakening of NO production in vascular wall. Probably, it takes place in the result of endothelial NO-syntheses suppression by strengthened LPO in plasma [43]. Forming in these conditions erythrocytes' micro rheological dysfunctions can worsen microcirculation processes and weaken tropism themselves, including vascular walls and production of disaggregates in them [44].

In present research the persons with hypodynamia were appointed regular adequate athletic physical loads for rehabilitation of a body. Against their background the examined persons had quantity decrease of lipids' peroxidation products in plasma and erythrocytes what promoted state optimization of these cells' membranes.

Noted weakening of erythrocytes' aggregation in the course of athletic trainings of persons with previous hypodynamia can be estimated as the result of the impact of physical activity rise on micro rheological processes. A decrease in the activity of lipid peroxidation resulted in a decrease in the blood of these people in the number of erythrocyte aggregates and a decrease in the degree of involvement in them of all new red blood cells. Detected weakening of erythrocytes' aggregation in the course of hypodynamia overcoming can be mostly explained by weakening of catecholamine's' impact on them, the level of which always lowers in their blood against the background of exercises [45].

The synthesis of biologically active substances able to limit erythrocytes' aggregation strengthened in vascular wall of persons who had hypodynamia earlier, against the background of started regular exercises. It was accompanied by level lowering of pro-aggregates in their blood. So, noted in the group of observation weakening of thromboxane formation and production strengthening of its functional antagonist – prostacyclin –was the start of imbalance restoration of arachidonic acid metabolites. Given process was supported by developing against this background strengthening of NO production in vascular wall [46]. Probably, it took place in the result of activation of endothelial NO-syntheses on behalf of progressive LPO weakening in plasma [47].

CONCLUSION

Persons of the second mature age who began athletic trainings after lasting hypodynamia are characterized by weakening of lipids' peroxidation processes in plasma. This is accompanied by a decrease in their aggregative capacity of red blood cells. This is accompanied by a decrease in their aggregation ability. The changes found can improve the rheology of blood in the capillaries and activate the atrophic in all internal organs, contributing to overall improvement. Considering incomplete recovery of erythrocyte aggregation after 6 months. physical training in previously avoided physical exertion of persons, it seems very important to continue physical activity with the mandatory control of their dynamics of erythrocyte aggregation.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

- [1] Skoryatina IA, Medvedev IN, ZavalishinaSYu. (2017) Ant platelet control of vessels over the main blood cells in hypertensive's with dyslipidemia in complex therapy. Cardiovascular therapy and prevention.16 (2):8-14.
- [2] ZavalishinaSYu, Medvedev IN. (2017) Comparison of opportunities from two therapeutically complexes for correction of vascular homeostasis in hypertensive are with metabolic syndrome. Cardiovascular therapy and prevention.16 (2):15-21.

- [3] Medvedev IN, NosovaTYu. (2007)Verospiron effects on platelet aggregation in patients with arterial hypertension and abdominal obesity. *Russian Journal of Cardiology*. 6:55-58.
- [4] Medvedev IN, Kumova TA. (2007) Vallarta effects on platelet activity in patients with arterial hypertension and metabolic syndrome. *Russian Journal of Cardiology*. 3:66-69.
- [5] Bikbulatova AA, Karplyuk AA, Tarasenko OV.(2017) Model of Activities of the Resource Training Center of the Russian State Social University in Terms of Professional Orientation and Employment of Persons with Disabilities. *Psikhologicheskayanaukaiobrazovanie*. 22(1):26-33.
- [6] Bikbulatova AA, Pochinok NB. (2017) Professional Skills Competitions for People with Disabilities as a Mechanism for Career Guidance and Promotion of Employment in People with Special Needs. *Psikhologicheskayanaukaiobrazovanie*. 22(1):81-87.
- [7] Medvedev IN. (2016) Platelet functional activity in rats, prolonged experiencing regular exercise. *VestnikSPbSU. Series 3.Biology*. 4: 99–107. doi: 10.21638/11701/spbu03.2016.407
- [8] ZavalishinaSYu, Medvedev IN. (2016) Features aggregation erythrocytes and platelets in old rats experiencing regular exercise on a treadmill. *Advances in gerontology*.29 (3):437-441.
- [9] Medvedev IN. (2016) Dynamics of violations of intravascular platelet activity in rats during the formation of metabolic syndrome using fructose models. *Problems of nutrition*. 85(1):42-46.
- [10] VatnikovYuA, ZavalishinaSYu, Pliushchikov VG, Kuznetsov VI, Seleznev SB, Kubatbekov TS, Rystsova EO, Parshina VI.(2017) Early-changes diagnostics of erythrocytes micro rheological features in the model of dyslipidemia development in rats at the late stages of ontogenesis. *Bali Medical Journal*. 6(1): 216-222. doi: 10.15562/bmj.v6i1.483
- [11] ZavalishinaSYu, Nagibina EV. (2012) Dynamics of microrheology characteristics of erythrocyte in children 7-8 years with scoliosis with therapeutic physical training and massage. *Technologies of Living Systems*. 9(4): 29-34.
- [12] Medvedev IN. (2016) Platelet functional activity in clinically healthy elderly. *Advances in gerontology*.29 (4):633-638.
- [13] Medvdev IN, Skoryatina IA, ZavalishinaSYu. (2016) Aggregation ability of the main blood cells in arterial hypertension and dyslipidemia patients on rosuvastatin and non-drug treatments. *Cardiovascular therapy and prevention*. 15(5):4-10.
- [14] VatnikovYuA, ZavalishinaSYu, Kulikov EV, Vilkovskiy IF, Nikishov AA, Drukovsky SG, Krotova EA, Khomenets NG, Bolshakova MV.(2017) Correctional abilities of regular muscle activity in relation to erythrocytes' micro rheological features of rats with experimentally developed hypertension. *Bali Medical Journal*. 6(3): 449-456.doi:10.15562/bmj.v6i3.586
- [15] ZavalishinaSYu. (2014) State regulation-vascular interactions in newborn piglets with iron with ferroglucin and glikopin. *Russian Agricultural Sciences*.1: 57-59.
- [16] Kotova OV, ZavalishinaSYu, Makurina ON, KipermanYaV, Savchenko AP, Skoblikova TV, Skripleva EV, Zacepin VI, Skriplev AV, AndreevaVYu.(2017) Impact estimation of long regular exercise on homeostasis and blood rheological features of patients with incipient hypertension. *Bali Medical Journal*. 6(3): 514-520. doi:10.15562/bmj.v6i3.552
- [17] Medvedev IN, Kumova TA. (2008)Eprosartan effects on intravascular platelet activity in patients with arterial hypertension and metabolic syndrome. *Russian Journal of Cardiology*. 1(69):40-42.
- [18] Medvedev IN, Amelina IV. (2009) AG polymorphism as a cytogenetic maker of arterial hypertension risk.*Russian Journal of Cardiology*.2 (76):70-72.
- [19] Medvedev IN, Danilenko OA. (2010) Comparative effects of therapeutic complexes on vascular wall activity in patients with arterial hypertension, metabolic syndrome, and recent ocular vessel occlusion. *Cardiovascular therapy and prevention*.9 (7):27-32.
- [20] Medvedev IN, Danilenko OA. (2010) Complex correction of vascular he most as is in patients with arterial hypertension, metabolic syndrome, and recent ocular vessel occlusion. *Russian Journal of Cardiology*.4: 15-19.
- [21] Medvedev IN, Mezentseva IN, Tolmachev VV. (2007) ACE inhibitors potential in correcting vessel wall anti-aggregation activity among patients with arterial hypertension and metabolic syndrome. *Russian Journal of Cardiology*. 1:48-52.
- [22] Medvedev IN, Kumova TA. (2007) Comparison of platelet homeostasis effects for angiotensin receptor blockers in patients with arterial hypertension and metabolic syndrome // *Russian Journal of Cardiology*. 4:52-56.
- [23] Medvedev IN, Kumova TA. (2007) Angiotensin II receptor inhibitors: role and place in arterial hypertension and metabolic syndrome treatment. *Russian Journal of Cardiology*. 5: 97-99.

- [24] Medvedev IN, Skoryatina IA. (2010) Platelet homeostasis dynamics in simvastatin-treated patients with arterial hypertension and dyslipidemia. *Russian Journal of Cardiology*. 1(81):54-58.
- [25] Medvedev IN. (2017) Microrheology of erythrocytes in arterial hypertension and dyslipidemia with a complex Hypolipidemic treatment. *Russian Journal of Cardiology*. 4(144):13-17.
- [26] Medvedev IN, Skoryatina IA. (2015) Aggregation properties of blood cells and vascular control over them in patients with arterial hypertension and dyslipidemia. *Russian Journal of Cardiology*. 4(120):18-22.
- [27] Medvedev IN, Skoryatina IA. (2014) Pravastatin in correction of vessel wall ant platelet control over the blood cells in patients with arterial hypertension and dyslipidemia. *Cardiovascular therapy and prevention*.13 (6):18-22.
- [28] Medvedev IN, Skoryatina IA. (2015)The aggregation capacity of neutrophils in patients with arterial hypertension and dyslipidemia treated with fluvastatin.*Klinicheskaiameditsina*.93 (1):66-70.
- [29] Volchegorskiy IA, Dolgushin II, Kolesnikov OL, Tseilikman VE.(2000) Experimental modeling and laboratory evaluation of adaptive reactions of the organism.*Chelyabinsk*, 167.
- [30] Metelskaya VA, Gumanova NG. (2005) Nitric oxide: a role in the regulation of biological functions, methods of determination in human blood. *Laboratory medicine*.7: 19-24.
- [31] Medvedev IN, Savchenko AP, ZavalishinaSYu, Krasnova EG, Kumova TA, Gamolina OV, Skoryatina IA, Fadeeva TS.(2009) Methodology of blood theology assessment in various clinical situations. *Russian Journal of Cardiology*. 5:42-45.
- [32] Gromnatskii NI, Medvedev IN. (2003) Non-pharmacological correction of impaired platelet homeostasis in hypertensive patients with metabolic syndrome). *Klinicheskaiameditsina*. 81(4):31-34.
- [33] Simonenko VB, Medvedev IN, Tolmachev VV. (2007) Comparative evaluation of the influence of sulfhydryl and phosphate ACE inhibitors on thrombolytic aggregation in patients suffering from arterial hypertension with metabolic syndrome. *Klinicheskaiameditsina*. 85(4):24-27.
- [34] Simonenko VB, Medvedev IN, Mezentseva NI, Tolmachev VV.(2007) The ant aggregation activity of the vascular wall in patients suffering from arterial hypertension with metabolic syndrome. *Klinicheskaiameditsina*. 85(7):28-30.
- [35] Medvedev IN. (2007) a comparative analysis of normodipin and spirapril effects on intravascular activity of platelets in patients with metabolic syndrome.*TerapevticheskiiArkhiv*. 79(10):25-27.
- [36] Medvedev IN, Gamolina OV. (2008)Lisinopril effects on platelet activity in patients with arterial hypertension and impaired glucose tolerance. *Russian Journal of Cardiology*.3:45-48.
- [37] Medvedev IN, Savchenko AP. (2010) Platelet activity correction by regular physical training in young people with high normal blood pressure. *Russian Journal of Cardiology*. 2(82): 35-40.
- [38] Medvedev IN, Skoriatina IA. (2010) Effect of lovastatin on adhesive and aggregation function of platelets in patients with arterial hypertension and dyslipidemia. *Klinicheskaiameditsina*. 88(2):38-40.
- [39] Medvedev IN, Skoryatina IA. (2014) Erythrocyte aggregation in patients with arterial hypertension and dyslipidemia treated with pravastatin. *Klinicheskaiameditsina*. 92(11):34-38.
- [40] ZavalishinaSYu, VatnikovYuA, Kulikov EV, Yagnikov SA, Karamyan AS, Sturov NV, Byakhova VM, Kochneva MV, Petryaeva AV.(2017) Diagnostics of erythrocytes' micro rheological features and early abnormalities of rats in the model of experimental hypertension development. *Bali Medical Journal*. 6(3): 470-475. doi:10.15562/bmj.v6i3.589
- [41] Glagoleva TI. (2017) Physiological features of vascular control over aggregation processes in the blood of repair heifers on the growth. *Zootekniya*. 5:14-16.
- [42] Glagoleva TI. (2015) vascular disaggregation control of major blood elements at calves on lacto-vegetable feeding. *Zootekniya*.5: 22-24.
- [43] Simonenko VB, Medvedev IN, Kumova TA. (2010) Path genetic aspects of hypertension in case of metabolic syndrome. *Voenno-meditsinskiizhurnal*. 331(9):41-44.
- [44] Medvedev IN, Skoryatina IA. (2013) Fluvastatin effects on blood cell aggregation in patients with arterial hypertension and dyslipidemia. *Cardiovascular Therapy and Prevention*. 12(2):18-24.
- [45] Simonenko VB, Medvedev IN, NosovaTYu. (2008) Aggregation function of platelets in persons with arterial hypertension and abdominal obesity. *Klinicheskaiameditsina*.86 (5):22-24.
- [46] Medvedev IN, Plotnikov AV, Kumova TA. (2008) Rapid normalization of platelet homeostasis in patients with arterial hypertension and metabolic syndrome. *Russian Journal of Cardiology*. 2:43-46.
- [47] Simonenko VB, Medvedev IN, Kumova TA. [2008] Effect of eprosartan on thrombocytes aggregative capacity in patients with arterial hypertension and metabolic syndrome. *Klinicheskaiameditsina*.86 (4):19-21.