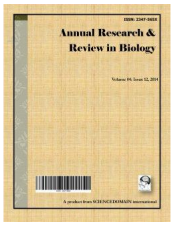

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Physiological Reaction of Erythrocytes' Micro Rheological Features in Newborn Piglets on Unfavourable Environmental Factors

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AVP and AAP designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors VIM and TIG managed the analyses of the study. Author NVK managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

The aim of research is to find out peculiarities of erythrocytes' micro rheological features in piglets having undergone the impact of the most abundant unfavourable factors of the environment. We observed 78 newborn piglets having undergone the impact of unfavourable environmental factors: 25 – prenatal iron deficiency, 28 – had undergone acute hypoxia at birth and 25 – had undergone super cooling with consequent development of dyspepsia. Control group was composed of 36 healthy newborn piglets. In our research biochemical, hematological and statistical methods of investigation were applied. There was found similar intensity increase of lipids' peroxidation against the background of comparable weakening of their antioxidant protect ability in blood plasma and

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erythrocytes of newborn piglets having undergone mentioned above unfavourable environmental factors. Newborn piglets with iron deficiency, after acute hypoxia and super cooling were found to have the rise of similar evidence of reversibly changed (approximately on 45%) and irreversibly changed (nearly in 2 times) erythrocytes' forms, rise of erythrocytes' involvement into aggregates on more than 40% and quantity rise of their aggregates on more than 30%. Under the impact of unfavourable environmental factors newborn piglets had activation of lipids' peroxidation in blood plasma and erythrocytes in the result of comparable weakening of their antioxidant protectability. Newborn piglets, which had undergone the impact of unfavourable environmental factors, had increased the quantity of erythrocytes' changed forms and strengthening of their ability to aggregation, the degree of which didn't depend on the character of preceded impact on their bodies.

Keywords: Newborn piglets; iron deficiency; acute hypoxia; super cooling; erythrocytes; aggregation; cytoarchitecture.

1. INTRODUCTION

Functioning of a body takes place in conditions of constant impact of various environmental factors [1,2]. Sometimes these impacts promote optimum disturbance of phenotypic manifestations of genetically determined [3] signs with development of dysfunctions and pathology [4,5]. One of very significant physiologically and vulnerable stages of ontogenesis is the newborn phase [6]. Microcirculation [7] is very important as it provides common functional adaptation of a body and its common resistance. It mostly determines the course of important vital processes of tissue metabolism [8,9] in all the tissues and common functional status of a body [10,11]. The most important components of microcirculation are regular blood elements, and the state of their micro rheological features directly determines its liquid peculiarities and the course of the processes of tissue metabolism [12,13].

It is known that aggregation and cytoarchitecture of regular blood elements in case of both animals and human beings keenly react on external and internal impacts which change parameters of a living being's functioning [14,15]. It becomes clear, that ontogenetic changes in a body cause changes in hemostasis and blood rheology and inevitably influence microcirculatory features of blood cells [16,17]. Notwithstanding the great successes of biology, many aspects of blood rheological features of biological objects [18,19,20] are not yet fully studied. Our task was to determine erythrocytes' micro rheological features in the course of newborn phase because of great functional significance of piglets' microcirculation in the course of the whole ontogenesis and possibility of its light disturbance at its beginning. It was decided to conduct estimation of dynamics of erythrocytes' aggregation and cytoarchitecture under the impact of most abundant unfavourable factors of the environment. The following negative environmental impacts influencing the state of erythrocytes' rheological features were chosen – iron deficiency, shortage of O_2 because of mechanical animal's squeeze at birth and casual short-time super cooling. They have led to the development of iron-deficiency anemia, acute hypoxia and dyspepsia which are widespread among newborn piglets.

The aim of our research is to find out peculiarities of erythrocytes' micro rheological features in piglets which have undergone the impact of most abundant unfavourable factors of the environment.

2. MATERIALS AND METHODS

The research was conducted in strict accordance with ethical principles established by the European Convent on protection of the vertebrata used for experimental and other scientific purposes (adopted in Strasbourg in March, 18th, 1986, and confirmed in Strasbourg in June, 15th, 2006) and approved by the local Ethics Committee of K. I. Skryabin Moscow State Academy of Veterenary Medicine and Biotechnology (record №14, dated December, 1st, 2015) and the local Ethics Committee of All-Russian Scientific Research Institute of Physiology, Biochemistry and Animals' Feeding (record №11, dated December, 4th, 2015).

We observed 114 newborn piglets of the breed "Large-White" which were kept on the farm "Verdazernoprodukt", Ryazan region (Russia). Seventy-eight of them were casually exposed to unfavourable impact of the environment (25 – had prenatal iron deficiency, 28 – had acute hypoxia at birth and 25 – had super cooling after birth with subsequent development of dyspepsia). Control group was composed of 36 healthy newborn piglets. All the animals were taken into the research on the 1st day of life.

All taken into the research newborn piglets were received from sows of the first or second farrowing with normal course of pregnancy.

All the animals were made morpho-biological blood analysis with the help of standard methods. It consisted of determining the quantity of erythrocytes, hemoglobin and concentration of serum iron.

Intensity of the processes of lipids' peroxidation (LPO) in liquid part of blood was estimated according to the content of thiobarbituric acid (TBA)-active products in it with the help of a set produced by the firm "Agat-Med" (Russia) and according to quantitative content of acylhydroperoxides (AHP) [21]. We also estimated antioxidant activity (AOA) of all the animals' blood plasma [21].

Erythrocytes were washed and resuspended by traditional method for estimation of their biochemical indices. Activity of LPO, going inside erythrocytes, was registered according to MDA level in the test of thiobarbituric acid reduction and according to the quantity of AHP in them [21]. Functional activity of antioxidant erythrocyte enzymes was determined for catalase and superoxide dismutase (SOD) [21].

Cytoarchitecture of erythrocytes was determined with the help of light phase-contrast microscopy. Erythrocytes were typed into ten classes (discocytes, discocytes with one outgrowth, discocytes with a crest, discocytes with numerous outgrowths, erythrocytes like mulberry, dome-shaped erythrocytes (stomatocytes), spherocytes with smooth surface, spherocytes with spinelets on the surface, erythrocytes like "deflated ball", degenerative forms of erythrocytes). The first 5 classes of erythrocytes (with signs of echinocytarous transformation) were considered to be reversibly deformed because of their ability to restore the form spontaneously. The rest classes were considered to be irreversibly deformed [22].

Aggregative activity of erythrocytes was registered with the help of light microscope by calculation of the number of erythrocytes' aggregates, aggregated and disaggregated erythrocytes in the meal of washed erythrocytes in Goryaev's box [23].

To find out the reliability of differences between experimental groups and control one we used Student's t-test. Statistical significance of differences was proved at $p<0.05$. The homogeneity of the data in the groups was checked by the magnitude of the coefficient of variation.

3. RESULTS AND DISCUSSION

All the indicators in the observed groups were homogeneous. The value of the coefficient of variation for them in the control group did not exceed 24%, in the group with iron deficiency - 25%, in the group of pigs that had acute hypoxia did not exceed 27%, and in the group of animals with dyspepsia it was not more than 28%.

Newborn piglets with inborn iron deficiency were noted to have disturbance of erythrogenesis against the background of level lowering of iron content in their blood in 2.3 times at the decrease of hemoglobin in it on 27.7% and erythrocytes - on 52.4%. Accountable red blood indices of newborn animals which had undergone acute hypoxia or dyspepsia, were in limits of the common norm. As for the rest accountable indices between groups of piglets having undergone unfavourable impacts, there were found no reliable differences.

We found reliable activation of plasma LPO in all the groups of examined animals after negative impact of the environment (Table 1). The level of TBA-active products in liquid part of blood in all three groups was nearly in 1.5 times higher than in control group. The content of AHP in their plasma also surpassed the control level more than in 2 times. Strengthening of peroxidation became possible in the result of weakening of a body's antioxidant protection – antioxidative plasma potential of newborn piglets with iron deficiency lowered till 28.1±0.03%, after acute hypoxia till 27.9±0.08%, at dyspepsia till 28.9±0.06% (in healthy animals it was equal to 37.3±0.13%).

Concentration of AHP in animals' erythrocytes with iron deficiency was higher in comparison with one of healthy piglets on 66.8%, after acute hypoxia on 61.6%, at dyspepsia on 64.0% what showed the activation of LPO initial stages in them. The level of MDA in erythrocytes was also higher on 51.5%, 55.5% and 53.5%, respectively (Table 1).

The increase of LPO processes in erythrocytes of newborn piglets after the impact of negative environmental factors was conditioned by lowering of their antioxidant protection. It was estimated according to the activity of catalase and superoxide dismutase. Their levels in all three groups of piglets, having undergone the impact of negative environmental factors, turned out to be lower on more than 30.0% and on more than 10.0%, respectively (Table 1).

Table 1. Accountable hematological indices of observed piglets

Registered parameters	Piglets with iron deficiency, n=25 M±m	Piglets after acute hypoxia, n=28 M±m	Piglets with dyspepsia after super cooling, n=25 M±m	Control, n=36, M±m
Number of red blood cells × 10^{12}/l	4.2±0.14 p<0.01	6.2±0.18 p<0.01 p_1<0.01	6.3±0.12 p<0.01 p_1<0.01	6.4±0.12
Hemoglobin, g/l	106.2±0.06 p<0.01	130.8±0.24 p<0.01 p_1<0.01	134.1±0.04 p<0.01 p_1<0.01	135.6±0.18
The level of iron in serum, umol /l	12.2±0.19 p<0.01	28.2±0.15 p<0.01 p_1<0.01	26.9±0.14 p<0.01 p_1<0.01	27.8±0.16
acyl hydroperoxides, D_{233}/1ml	3.14±0.05 p<0.01	2.99±0.09 p<0.01	3.14±0.04 p<0.01	1.32±0.11
TBA-active products, umol/l	5.06±0.08 p<0.01	4.86±0.06 p<0.01	4.99±0.08 p<0.01	3.06±0.12
antioxidant activity plasma, %	27.5±0.04 p<0.01	27.9±0.08 p<0.01	28.9±0.06 p<0.01	37.3±0.13
acylhydroperoxides of erythrocytes, $D_{233}/10^{12}$ erythrocytes	4.80±0.16 p<0.01	4.72±0.12 p<0.01	4.79±0.15 p<0.01	2.92±0.05
malon dialdehyde of erythrocytes, nmol/10^{12} erythrocytes	1.54±0.13 p<0.01	1.54±0.09 p<0.01	1.52±0.09 p<0.01	0.99±0.06
catalase of erythrocytes, ME/10^{12} erythrocytes	7980.0±39.2 p<0.01	8240.5±19.9 p<0.01	8180.6±31.4 p<0.01	10968.0±16.6
superoxide dismutase of erythrocytes, ME/10^{12} erythrocytes	1497.0±10.63 p<0.01	1493.1±9.26 p<0.01	1502.1±9.62 p<0.01	1718.0±5.72
erythrocytes-discocytes,%	72.5±0.32 p<0.01	72.8±0.12 p<0.01	72.1±0.16 p<0.01	85.3±0.17
reversibly modified erythrocytes,%	14.9±0.16 p<0.01	14.6±0.16 p<0.01	13.9±0.17 p<0.01	9.3±0.06
irreversibly modified erythrocytes,%	12.6±0.09 p<0.01	12.6±0.05 p<0.01	14.0±0.06 p<0.01	5.3±0.06
sum of all the erythrocytes in an aggregate	48.1±0.29 p<0.01	48.8±0.17 p<0.01	47.2±0.26 p<0.01	32.3±0.08
quantity of aggregates	9.9±0.06 p<0.01	12.6±0.09 p<0.01	11.9±0.08 p<0.01	7.2±0.04
quantity of free erythrocytes	232.8±0.19 p<0.01	232.6±0.39 p<0.01	240.2±0.25 p<0.01	282.3±0.19

Conventional Sign: p – reliability of differences between observed groups and control group, p_1 – reliability of differences between the group of observed piglets with iron deficiency and two other groups. Reliability of differences between indices of piglets with dyspepsia and after acute hypoxia was not received.

Newborn animals after negative impact of the environment were noticed to have evident level lowering of discoid formed erythrocytes in blood (Table 1). It was accompanied by reliable rise of summary quantitative content of erythrocytes' reversibly and irreversibly changed forms on more than 45% and in more than 2 times, respectively.

Newborn animals after the impact of negative environmental factors were found to have strengthening of erythrocytes' aggregation (Table 1). So, these piglets had evident rise of erythrocytes' involvement into aggregates (on more than 40.0%) and quantity of aggregates themselves in blood (on more than 30.0%) at reliable content lowering of freely moving erythrocytes in it.

At present different aspects of hemostasis and blood rheology of separate biological objects are being actively studied [24,25]. At the same time, the impact of negative factors on blood rheology of piglets isn't yet fully studied. Iron deficiency, acute hypoxia and dyspepsia in newborn productive animals are still rather often met states which cause essential economic loss in the result of murrain and weakening of livestock population [26].

At given unfavourable impacts the newborn piglets had comparable lowering of antioxidant protectability of blood plasma leading to similar quantity increase of initial LPO-AHP products and secondary LPO-TBA-active products. It worsened already disturbed processes of metabolism. Found intensity increase of plasma LPO processes inevitably caused damage of erythrocytes' external membranes what additionally worsened their functions and conditioned negative dynamics of their surface geometry and strengthened their ability to unite into aggregates [27,28].

The newborn piglets after the impact of negative environmental factors were noticed to have similar changes in a body what was determined by their genetic program [29]. So, their erythrocytes had similar depression of antioxidative enzymes leading to the increase of LPO intensity in them. Developing metabolic disturbances in their erythrocytes caused additional depression strengthening of their antioxidant protection [30,31]. It was confirmed by the results of functional activity estimation of catalase and superoxide dismutase in them.

It was found in the research LPO activation damaged lipid bilayer of their membranes from the inside and outside. Formed situation inevitably caused irreversible disturbances of structural-functional status of some erythrocytes [32]. It led to the loss of biconcave form by many erythrocytes what worsened their ability to move along small vessels. So, some erythrocytes of newborn piglets in conditions of iron deficiency, after acute hypoxia or super cooling began to get transformed to the same extent into spheres with signs of echinocytosis (the surface of erythrocytes was covered by conical journals) and stomatocytosis (erythrocytes were like unilaterally arched disks). Further changes of the form of piglets' erythrocytes after the impact of negative environmental factors on their bodies inevitably went through the stages of sphero-echinocytosis and sphero-stomatocytosis. The final stage of transformation – spherecyte – was the most rigid structure which usually preceded break-up of a cell [33] stimulating hemostasis processes at that [34,35].

It was found phenomenon of comparable growth of erythrocytes' aggregation in newborn piglets at iron deficiency, acute hypoxia and dyspepsia was mostly connected with similar charge changing of erythrocytes because of degradation of proteins with negative charge on their surface in the result of LPO strengthening [36]. Similar activation of active oxygen forms' formation at these states also caused oxidative damages of plasma globular proteins which played the role of "bridges" between erythrocytes in the course of their aggregation. It promoted the increase of linkage force between erythrocytes in aggregates [37,38]. It caused changes in erythrocytes' forms till hemolysis in the result of oxidation of membrane's lipids. At the same time, LPO products caused evident increase of the threshold of erythrocytes' disaggregation in conditions of the impact of any negative environmental factor regardless of its character. It increased the force of erythrocytes' linkage in aggregates and raised the speed of aggregation [39].

It was found worsening of cytoarchitecture and rise of erythrocytes' aggregative ability in newborn piglets, having undergone negative impacts of environmental factors, inevitably led to disturbance of microcirculation in all the internals [40]. The irreversible aggregation promoted erythrocytes' damage and release of coagulation factors into blood. Surplus erythrocytes' aggregation blocked bloodstream inside vessels and, that is why, part of small vessels could be fully occluded. Erythrocytes' aggregates as lightly disintegrating "coined columns" and their dense, nonvolatile conglomerates could play the role of embolus [41,42]. Developing erythrocytes' hyper aggregation in these conditions damaged normal bloodstream in micro vessels, leading to microcirculatory block and deepening tissue hypoxia [43,44]. It was an important factor which caused similar changes of metabolism in tissues of newborn piglets regardless of the character of negative environmental impact on them.

4. CONCLUSION

Under the impact of unfavourable environmental factors newborn piglets have activation of lipids' peroxidation in blood plasma and erythrocytes in the result of comparable weakening of their antioxidant protectability. Newborn piglets, which have undergone the impact of unfavourable environmental factors, have quantity rise of erythrocytes' changed forms and strengthening of their ability to aggregation, the degree of which doesn't depend on the character of preceded impact on their bodies.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Medvedev IN, Gromnatskii NI. Correction of thrombocyte hemostasis and biological age reduction in metabolic syndrome. Klinicheskaia Meditsina. 2005;83(8):54-57.
2. Medvedev IN, Gromnatskii NI. Effect of amlodipine on intravascular thrombocyte activity in patients with arterial hypertension and metabolic syndrome. Klinicheskaia Meditsina. 2005;83(2):37-39.
3. Amelina IV, Medvedev IN. Transcriptional activity of chromosome nucleolar organizing regions in population of Kursk region. Bulletin of Experimental Biology and Medicine. 2009;147(6):730-732.
4. Medvedev IN, Kumova TA. Reduced platelet aggregation in losartan-treated patients with arterial hypertension and metabolic syndrome. Russian Journal of Cardiology. 2008;1:40-42.
5. Medvedev IN, Skoriatina IA. Effect of lovastatin on adhesive and aggregation function of platelets in patients with arterial hypertension and dyslipidemia. Klinicheskaia Meditsina. 2010;88(2):38-40.
6. Zavalishina SYu, Medvedev IN. Comparison of opportunities from two therapeutical complexes for correction of vascular hemostasis in hypertensives with metabolic syndrome. Cardiovascular Therapy and Prevention. 2017;16(2): 15-21.
7. Gromnatskii NI, Medvedev IN. Non-pharmacological correction of impaired platelet hemostasis in hypertensive patients with metabolic syndrome. Klinicheskaia Meditsina. 2003;81(4):31-34.
8. Medvedev IN, Zavalishina SYu. Platelet activity in patients with third degree arterial hypertension and metabolic syndrome. Kardiologiia. 2016;56(1):48.
9. Zavalishina SYu, Kutafina NV, Vatnikov YUA, Makurina ON, Kulikov EV. Platelet-activity dependence on the age of rats with experimental dyslipidemia. Biol Med (Aligarh). 2016;8:326. DOI: 10.4172/0974-8369.1000326
10. Simonenko VB, Medvedev IN, Tolmachev VV. Comparative evaluation of the influence of sulfhydryl and phosphate ACE inhibitors on thrombocyte aggregation in patients suffering from arterial hypertension with metabolic syndrome. Klinicheskaia Meditsina. 2007;85(4):24-27.
11. Sizov AA, Zavalishina SJ. Russian criminal legislation in prevention of sexually transmitted diseases in the territory of the Russian Federation. Biology and Medicine (Aligarh). 2015;7(5):142-15.
12. Medvedev IN, Gromnatskii NI. The influence of nebivolol on thrombocyte aggregation in patients with arterial hypertension with metabolic syndrome. Klinicheskaia Meditsina. 2005;83(3):31-33.
13. Medvedev IN, Gromnatskii NI. The influence of hypocaloric diet on thrombocyte rheology in patients with metabolic syndrome. Klinicheskaia Meditsina. 2006;84(3):49-52.
14. Medvedev IN, Lapshina EV, Zavalishina SYu. Experimental methods for clinical practice: Activity of platelet

hemostasis in children with spinal deformities. Bulletin of Experimental Biology and Medicine. 2010;149(5):645-646.

15. Simonenko VB, Medvedev IN, Mezentseva NI, Tolmachev VV. The antiaggregation activity of the vascular wall in patients suffering from arterial hypertension with metabolic syndrome. Klinicheskaia Meditsina. 2007;85(7):28-30.
16. Zaitsev SY, Milaeva IV, Zarudnaya EN, Maximov VI. Investigation of dynamic surface tension of biological liquids for animal blood diagnostics. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2011;383(1-3):109-113.
17. Kutafina NV, Medvedev IN. Platelet aggregation in clinically healthy persons of the second coming of age living in Kursk region. Advances in Gerontology. 2015;28(2):321-325.
18. Generalova AN, Marchenko SB, Gorokhova IV, Zaitsev SYu, Miller R, Gurevich IV, Tsarkova MS, Maksimov VI. Advantages of interfacial tensiometry for studying the interactions of biologically active compounds. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2007;298(1-2):88-93.
19. Amelina IV, Medvedev IN. Relationship between the chromosome nucleoli-forming regions and somatometric parameters in humans. Bulletin of Experimental Biology and Medicine. 2009;147(1):77-80.
20. Zaitsev SY, Maksimov VI, Bardyukova TV. Supramolecular enzymatic systems of the dog blood: Clinical diagnostic implications. Moscow University Chemistry Bulletin. 2008;63(2):99-102.
21. Bikbulatova AA. Determining the thickness of materials in therapeutic and preventive heat-saving garments. Proceedings of higher education institutes. Textile Industry Technology. 2014;1(349):119-123.
22. Medvedev IN, Savchenko AP, Zavalishina SYu, Krasnova EG, Kumova TA, Gamolina OV, Skoryatina IA, Fadeeva TS. Methodology of blood rheology assessment in various clinical situations. Russian Journal of Cardiology. 2009;5:42-45.
23. Medvedev IN, Maksimov VI, Parakhnevich AV, Zavalishina SYu, Kutafina NV. Rapid assessment of aggregation abilities and surface properties of platelets and red blood cells. International Journal of Pharma and Bio Sciences. 2016;7(2):(B) 793-797.
24. Zavalishina SYu. Physiological dynamics of spontaneous erythrocytes' aggregation of rats at last ontogenesis. Annual Research & Review in Biology. 2017;13(1): 1-7.
DOI: 10.9734/ARRB/2017/33616
25. Glagoleva TI, Zavalishina SYu. Aggregative activity of basic regular blood elements and vascular disaggregating control over it in calves of milk-vegetable nutrition. Annual Research & Review in Biology. 2017;12(6):1-7.
DOI: 10.9734/ARRB/2017/33767
26. Zavalishina SYu. Physiological features of hemostasis in newborn calves receiving ferroglukin, fosprenil and hamavit, for iron deficiency. Annual Research & Review in Biology. 2017;14(2):1-8.
DOI: 10.9734/ARRB/2017/33617
27. Medvedev IN, Skoriatina IA. Dynamics of microrheologic properties of erythrocytes in patients with arterial hypertension and dyslipidemia treated with atorvastatin. Klinicheskaia Meditsina. 2012;90(6):42-45.
28. Medvedev IN, Skoryatina IA. Fluvastatin effects on blood cell aggregation in patients with arterial hypertension and dyslipidemia. Cardiovascular Therapy and Prevention. 2013;12(2):18-24.
29. Medvedev IN, Amelina IV. An association between human morphological phenotypical characteristics and the activity of chromosomal nucleolar organizer regions in the interphase cell nucleus in the population of indigenous people of Kursk region. Morfologii. 2012; 142(4):87-91.
30. Simonenko VB, Medvedev IN, Tolmachev VV. Effect of irbesartan of the function of hemocoagulative component of hemostasis in patients with arterial hypertension during metabolic syndrome. Klinicheskaia Meditsina. 2010;88(6):27-30.
31. Zavalishina SYu, Vatnikov YuA, Makurina ON, Kulikov EV, Sotnikova ED, Parshina VI, Rystsova EO, Kochneva MV, Sturov NV. Diagnostical appreciation of physiological reaction of intravascular thrombocytes activity of two-years-old mice to regular physical loads. Biomedical & Pharmacology Journal. 2017:10(1):129-136.
Available:http://dx.doi.org/10.13005/bpj/1090

32. Medvedev IN. Microrheology of erythrocytes in arterial hypertension and dyslipidemia with a complex hypolipidemic treatment. Russian Journal of Cardiology. 2017;4(144):13-17.
33. Medvedev IN, Kumova TA. Reduced platelet aggregation in losartan-treated patients with arterial hypertension and metabolic syndrome. Russian Journal of Cardiology. 2008;5:53-55.
34. Simonenko VB, Medvedev IN, Kumova TA. Pathogenetic aspects of hypertension in case of metabolic syndrome. Voenno-Meditsinskii Zhurnal. 2010;331(9):41-44.
35. Simonenko VB, Medvedev IN, Tolmachev VV. Pathogenetic aspects of arterial hypertension in metabolic syndrome. Klinicheskaia Meditsina. 2011;89(1):49-51.
36. Medvedev IN. Dynamics of violations of intravascular platelet activity in rats during the formation of metabolic syndrome using fructose models. Problems of Nutrition. 2016; 85(1):42-46.
37. Simonenko VB, Medvedev IN, Gamolina OV. Primary hemostasis activity in patients with arterial hypertension and impaired glucose tolerance treated with trandolapril. Klinicheskaia Meditsina. 2011;89(2):29-31.
38. Simonenko VB, Medvedev IN, Tolmachev VV. Dynamics of primary hemostasis activity in patients with arterial hypertension and metabolic syndrome treated with candesartan. Klinicheskaia Meditsina. 2011;89(3):35-38.
39. Medvedev IN, Bryukhovetsky AG. The use of verospiron and the degree of platelet aggregation in arterial hypertension with abdominal obesity. Klinicheskaia Meditsina. 2014;92(3):50-53.
40. Medvedev IN, Danilenko OA. Effectiveness of vascular wall activity correction in patients with arterial hypertension, metabolic syndrome, and oculo-vascular occlusion. Russian Journal of Cardiology. 2010;83(3):64-67.
41. Simonenko VB, Medvedev IN, Kumova TA. Losartan for correction of thrombocyte activity in patients suffering from arterial hypertension with metabolic syndrome. Klinicheskaia Meditsina. 2008;86(1):38-41.
42. Medvedev IN, Skoryatina IA. Pravastatin in correction of vessel wall antiplatelet control over the blood cells in patients with arterial hypertension and dyslipidemia. Cardiovascular Therapy and Prevention. 2014;13(6):18-22.
43. Kutafina NV, Medvedev IN. Platelet aggregation in clinically healthy persons of the second coming-of-age living in the Kursk Oblast. Advances in Gerontology. 2015;5(4):267-270.
44. Medvedev IN. Vascular-platelet interaction in pregnant cows. Bulg. J. Agric. Sci. 2017; 23(2):310-314.

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