PROTEIN-LIPID COMPOSITION OF ERYTHROCYTE MEMBRANES AND METABOLISM IN CHRONIC ENDOMETRITIS

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Background: *Establishment of changes in protein-lipid spectrum of erythrocyte's membrane in CE before and after traditional complex treatment.*

Materials and methods: *At 38 patients in reproductive age with verified diagnosis of chronic endometritis in stage of incomplete remission, treated by traditional treatment complex, what included surgical intervention about sterility, were studied parameters of structural-functional properties of erythrocytes before and after treatment.*

Results. *Before treatment were established considerable changes in composition of proteins, what is in charge for structure formation and stabilization of erythrocyte's membrane (α- and β-spectrin, dematin, ancirin, protein of a strip 4.1, pallidin), formation and flexibility of membrane (actin, tropomyosin), intracellular metabolism (anion-transporting protein, glyceraldehyde-3-phosphate dehydrogenase, glutathione-S-transferase). Were revealed disorders in maintenance and correlation of lipid spectrum, in the first place lowering of maintenance of membrane glycerophospholipids and sphingomyelins, what form base of double lipid carcass of cell membrane and play main role in arrangement of protein macromolecules and normal metabolism of erythrocytes. Defined intracellular increase of lipids peroxidation processes and maintenance of nitrogen oxides stable metabolites, lowering of activity of antioxidant defense. After treatment 9% of changed before treatment parameters were normalized, corrected, but not to normal reference ranges, 55,6%, 33,4% of indices remained the same.*

Keywords: *chronic endometritis; disorders of structural-functional properties of erythrocytes; protein-lipid composition of erythrocyte membranes.*

Introduction

Chronic endometritis (CE), despite the multiplicity of studies and information about its significant prevalence (60–65%), continues to draw attention of domestic and foreign specialists. At present time actuality of the problem of this disease takes not only medical, but social significance, as far as this disease often leads to disturbance of reproductive function, is a reason of sterility, unsuccessful attempts of extracorporeal fertilization (in vitro fertilization), noncarrying of pregnancy, complicated course of pregnancy and act of delivery [1, pp. 690–695, 2, pp. 40–45].

At the present time CE is viewed as complex undulatory inflammatory process, during which goes activation of wide spectrum of factors, that induce cascade damages with involvement of different structures. Against the background of durative inflammatory process in endometrium forms self-sustaining pathological system with intense sclerotic processes, damaging of extracellular matrix, disorder in mediator cell-cell collaboration, change in angioarchitectonics of tissues and ischemia. On this background immune barrier of uterine mucosa is defective and opportunistic pathogenic microflora in uterine cavity with the lapse of time might become leading microbial factor of chronic endometritis aggravation [2, pp. 40–45, 3, pp. 289–307, 4, pp. 16–18].

Known disorders of maintenance and correlation of proteins and lipids in erythrocyte's membrane in gynecological diseases [5, pp. 5–36], but considering, that literature doesn't cover pathogenetic role of erythrocytes in appearance and development of CE and not studied ability of pharmacological correction of this disorders, the aim of present study became establishment of changes in protein-lipid spectrum of erythrocyte's membrane in CE before and after traditional complex treatment.

Materials and methods

Under constant observation in gynecological department of Kursk municipal maternity hospital were placed 38 patients of reproductive

age (18–35 years old). Inclusion of patients in study realized basing on informed consent. All of the patients got complex clinical-instrumental examination according to generally accepted standards, at that, in all cases verification of diagnosis of chronic endometritis in stage of incomplete remission took place. All of the women had concomitant diseases or they were in stage of remission, they all got endoscopic operative intervention on subject of endometritis-associated sterility. In post-operative period patients got traditional treatment. Also were studied laboratory indices in erythrocytes of 16 healthy women of the same age, who formed control group.

Before the start of complex treatment and after it were received erythrocytes from 10 ml of heparinized blood, after centrifugation separated plasm, and erythrocytic mass subjected to filtration on chromatographic column through HBS-cellulose, after that defined adsorption ability of erythrocytes (AAE) [6, pp. 22–24] and of their glycocalix adsorption capacity (GAC) [7, pp. 113–118]. Membranes of erythrocytes were extracted by method of G.T. Dodge [8, pp. 119–130], membrane's lipids were defined by method of thin-layer chromatography [9, pp. 205–206]. Electrophoresis of proteins was made in presence of sodium dodecyl sulfate in vertical plates of polyacrylamide gel following the method of U.K. Laemmli [10, p. 680], proteins were dyed by Coomassie blue R-250. Intensity of lipid peroxidation processes (LP) evaluated by maintenance of acyl hydroperoxides (AGP) and malondialdehyde (MDA) in erythrocytes, that form dyed complex with c thiobarbituric acid. Definition of MDA and AGP were made with help of kit «TBK-Agat » («Agat-Med» Russia), while using of spectrophotometer «Apel-330» (Japan) on 535 nm and 570 nm wavelength. For assessment of the state of antioxidant system were defined by method of straight/concurrent enzyme-linked immunosorbent assay (ELISA) with detection of reaction products in range of 405–630 wavelength with application of pre-made commercial sets: activity of superoxide dismutase (SOD) «Bender Medsystems» (Austria) and catalase «Cayman Chemical» (USA). General antioxidant activity

(GAA), defined by the method, that is based on degree of inhibition of ascorbate- and ferroinduced oxidation of tween-80 to MDA. Level of stable nitrogen oxide metabolites (CM_{ON}) was discovered with use of two analytic operations: measuring of endogenous nitrite and transformation of nitrate into nitrite with use of nitrite reductase with following measuring of common nitrite by absorption of azo dye in Griess reaction on 540 nm wavelength with application of commercial set for ELISA from «R&D» company (England). Registration of all of the ELISA results was made with the help of microplate photometer «Sunrise», Tecan (Austria).

Statistical analysis of results of the study were made following generally accepted criteria of variational-statistical analysis with calculation of middle amounts (M), standard error of mean (m) with the help of package of computer programs Microsoft Excel, 2010. Severity of differences was judged by Mann Whitney U-test. Differences was counted statistically meaningful if $p < 0,05$.

Results of study and its discussion

In CE before treatment was established lowering in erythrocyte's membrane of α- and β-spectrin, ancirin, anion transport protein (ATP), pallidin, dematin, glyceraldehyde-3-phosphate dehydrogenase (G-3-PD) and glutathione-S transferase (G-S T), increasing of maintenance of protein of a strip 4.1, actin and tropomyosin in the presence of protein of a strip 4.5 normal level. Operative and pharmacological treatment normalizes representativeness of α- and β-spectrin and tropomyosin in erythrocyte's membrane, corrects, but not to normal parameters, maintenance of ancirin, pallidin, dematin and actin, does not effect on level of ATP, protein of a strip 4.1, G-3-PD and G-S T (table 1).

At admission to the clinic at the patients with CE was discovered decrease in phosphatidylcholine (PC), phosphatidylserine (PS), phosphatidylinositol (PI), glycerophospholipids (GPL – sum of LPC, PC, PE, PS and PI), sphingomyelin (SM), phospholipids (PL – sum of GPL and SM), increase in lysophosphatidylcholine (LPC), cholesterol (C),

ethers of cholesterol (EC) and triacylglycerol (TAG), in the presence of normal concentration of phosphatidylethanolamine (PE), sum of mono- and diacylglycerol (MAG, DAG) and non-etherified fatty acids (NEFA). Complex treatment approaches to the parameters of healthy donors' indices of LPC, PS, PI, GPL, SM and PL, but does not effect on representativeness of PC, C, EC and TAG (table 2).

Table 1.

Proteins of erythrocyte's membrane at the patients with CE before and after treatment (M±m)

Indices	1	2	3
	Healthy	Patients	
		Before treatment	After treatment
α-spectrin	102,4±2,7	92,8±2,3*1	97,4±2,0*2
β-spectrin	120,1±3,6	102,9±2,4*1	119,5±2,5*2
Ancirin	94,2±1,6	37,8±1,9*1	46,6±2,4*1,2
ATP	175,4±3,3	191,6±4,3*1	193,5±3,7*1
4.1	42,4±1,6	82,5±1,7*1	78,2±1,9*1
Pallidin	92,4±2,8	47,4±1,4*1	59,4±2,2*1,2
4.5	101,5±2,7	107,4±4,5	102,1±3,9
Dematin	68,3±1,9	21,9±1,1*1	31,9±1,8*1,2
Actin	78,5±1,6	90,4±1,9*1	84,4±2,2*1,2
G-3 PD	47,8±2,1	29,3±1,5*1	32,5±1,8*1
Tropomyosin	48,7±1,5	62,9±2,1*1	50,2±1,7*2
G-S T	68,6±1,4	47,2±1,3*1	51,6±2,3*1

Note: on this one and tables 2 and 3 authentic differences of arithmetical mean ($p < 0,05$) marked with a star; numbers next to the star – relatively to indices of which group mean relates to. In this and table 2 units of indices – mg%

In analysis of correlation of studied lipid fractions in erythrocyte's membrane was established, what before treatment in CE increases correlation LPC/PC, SM/PC, SM/PC, PC/PS and C+EC/PL, but lowers correlation of PC/PE and PC/PE+PS+PI. After treatment normalizes correlation of PC/PS, corrects to the side of control indices correlation of LPC/PC, SM/PC, PC/PE and C+EC/PL, remains the same correlation of SM/PC и PC/PE +PS+PE (table 2).

At the patients with CE before the start of treatment in erythrocytes was established activation of lipid peroxidation processes (LP, increase in concentration of MDA and AGP), lowering of antioxidant defense factors (ADF, activity of SOD and catalase). Besides, established increase in CM_{ON} and decrease in absorption indices of erythrocyte's membrane (GAC and AAE). Treatment did not effect on changed indices of antioxidant defense of erythrocytes (SOD and ADF) and corrected to the side of healthy donors indices all of the others studied indices of metabolic activity of erythrocytes (table 3).

Таблица 2.

Lipids of erythrocyte's membrane at the patients with CE before and after treatment (M±m)

Indices	1	2	3
	Healthy	Patients	
		Before treatment	After treatment
PC	28,1±0,8	19,5±0,7*1	20,9±1,1*1
LPS	4,2±0,1	6,4±0,09*1	5,4±0,1*1,2
PE	24,0±1,0	24,2±0,9	23,4±1,4
PS	28,4±0,9	17,5±0,7*1	22,1±1,1*1,2
PI	4,5±0,06	3,8±0,04*1	4,1±0,06*1,2
GPL	89,2±2,7	71,4±1,9*1	75,9±1,7*1,2
SM	14,1±0,5	11,9±0,6*1	12,7±0,7*1,2
PL	103,3±3,3	83,3±2,4*1	88,6±1,9*1,2
C	32,4±1,1	40,5±1,4*1	38,9±1,8*1
EC	28,1±1,2	35,9±1,4*1	32,3±2,2*1
TAG	13,2±0,6	16,5±0,5*1	17,3±1,1*1
DAG+MAG	11,0±0,4	10,0±0,6	10,5±0,7
NEFA	2,9±0,1	2,8±0,04	3,0±0,1
Correlation of lipid fractions			
LPS/PC	0,15±0,02	0,33±0,03*1	0,26±0,02*1,2
SM/PC	0,5±0,03	0,61±0,03*1	0,61±0,02*1
SM/PS	0,5±0,01	0,68±0,04*1	0,57±0,02*1,2
PC/PE	1,17±0,03	0,81±0,02*1	0,89±0,03*1,2
PC/PS	0,99±0,03	1,11±0,02*1	0,96±0,04
PC/PE+ PS+PI	0,49±0,02	0,43±0,02*1	0,42±0,02*1
C/PL	0,59±0,02	0,92±0,04*1	0,8±0,03*1,2

Table 3.

Metabolic indices of erythrocytes in CE before and after treatment (M±m)

Indices	Units	1	2	3
		Healthy	Patients	
			Before treatment	After treatment
MDA	mkmol/l	0,39±0,03	1,1±0,07*1	0,7±0,04*1,2
AGP	UE	0,22±0,02	0,89±0,04*1	0,76±0,02*1,2
ADF	%	35,1±3,0	25,6±2,8*1	27,0±1,9*1
SOD	UE	18,9±0,9	14,1±1,1*1	15,2±1,7*1
Catalase	mkcat/l	24,1±1,1	17,6±2,2*1	20,1±2,3*1,2
CM_{NO}	mkmol/l	2,4±0,2	4,9±0,1*1	4,1±0,2*1,2
GAC	10^{-12} g/er.	1,8±0,06	1,3±0,04*1	1,5±0,05*1,2
AAE	%	33,1±1,8	18,5±1,9*1	22,7±1,4*1,2

In such a way, can be stated, what at the patients with CE before the start of treatment occurred to be changed 90% of parameters, comparing to the indices of structural-functional properties of healthy donors' erythrocytes. Complex traditional treatment normalized 9% of parameters, changed before, corrected, but not to normal indices, 55,6%. Without change remained 33,4% of indices (table 1–3).

Membrane of erythrocyte makes only 1% of its weight, although her role in life of a red blood cell is extremely big. Membrane provides elasticity of erythrocyte, strength, durability, ability for stretching during penetration through narrow openings and canals, supports intracellular homeostasis and functional condition of erythrocyte. Although general structural peculiarities of biological membrane of erythrocytes are defined by properties of lipid bilayer, and most of her specific functions realized by proteins. Defining factor of smooth functioning of erythrocyte's membrane, is strict order of protein macromolecules placement. Major part (up to 80%) of peripheral proteins in erythrocyte's membrane is also a part of its cytoskeleton, which is an elastic two-dimensional net, connected directly to membrane through the interaction with polar groups of integral proteins and polar heads of lipids. Besides, to peripheral proteins relates a set of erythrocytic enzymes [11, pp. 471–476, 12, pp. 7–27].

The data obtained that there are significant changes from the proteins side, what are liable for structure formation and stabilization of erythrocyte's membrane (α- and β-spectrin, dematin – general proteins of cytoskeleton, ancirin, protein of a strip 4.1, pallidin), formation and flexibility of membrane (actin, tropomyosin), intracellular metabolism (G-3 PD, G-S T).

Membranes of erythrocytes contain inner and outer layers of PL, but, distribution of its individual representatives in membrane is asymmetrical. Choline-containing neutral by the charge PC and SM placed mainly in outer monolayer of membrane, whereas aminophospholipids – PE and PS, as well as PI which does not contain nitrogen, mainly placed in inner layer. A fundamental role in preservation of bilayer organization of biological membranes play PC and SM. PC has high exchanging activity and a significant meaning for penetrability of membrane, influents on metabolism of C and play a special regulatory role in processes of LP in norm and also in development of pathological conditions. Correlation of SM and PC defines not only osmotic and hemolytic steadiness of erythrocytes, but also their thermostability and duration of circulation in bloodstream. PC and PE are specific activators of a row of membrane-bound enzymes, what effect on stem cells, increase formation of the hotbeds of haemopoiesis, activate a system of mononuclear phagocytes, provide an antioxidant activity of lipids in erythrocyte's membrane. Presence of PC is necessary for a normal functioning of most isoforms of protein kinase C, but also Na^+/ K^+-ATPase, neutral sphingomyelinase and other enzymes. PC plays exceptionally important role in process of erythrocyte's apoptosis (erythroptosis), which is one of the ways of blood cells' rejuvenation. Selective oxidation of PC and its further transfer in outer part of membrane assists to recognition and destruction of similar cells by macrophages and its further elimination from circulating blood [13, pp. 3–7, 14, pp. 334–354, 15, pp. 587–602].

Important role in regulation of metabolism plays PI, despite low concentration of PL in erythrocytes. Moreover, in lots of cell processes, acting as secondary messengers, participate products of PI decay. Accumulation of PI in membranes increases ability of control over

the transport and information transmission into the cell in the form of humoral signals. Differences in metabolism and composition of PI in erythrocyte's membrane influences on physical-chemical properties of membrane, particularly, on its viscosity and ability for bounding of calcium ions, what in its turn determinants changes of membrane's functions. On the outer surface of erythrocyte's membrane are lysoformes of PL, particularly, LPC, what takes part in regulation of activity of connected to membrane enzymes, is a secondary transmitter of transmembrane signaling inside the cell. Variations of LPC maintenance can lead to a change in topology of membrane system – appearance of pores. Excessive amount PL hydrolysis – NEFA and PL lysoformes – powerful factor of modification of lipid bilayer and integral membrane proteins' properties. Cytolytic effect of LPC, what is accompanied with increasing of membrane's penetrability for organic molecules and ions, conditioned by combination of their action as a surface-active compounds and ionophores, what causes structural reorganizations of lipid component and proteins in membranes [12, pp. 7–27, 15, pp. 587–602, 16, pp. 97–118, 17, pp. 442–447].

Molecules of C are scattered on outer side in such a way, so their maintenance equals approximately one molecule of C on each molecule of PL. Presence of C in bilayer assists to elongating of saturated and unsaturated chains of PL molecules, tightening of bilayer, decreases penetrability for small water-soluble molecules and water, increases elasticity and mechanical strength of bilayer, changes activity of membrane proteins. Due to C membrane can change its form, answering to the applied force, but unlikely from PL, cholesterol can rapidly redistribute between monolayers. Although C makes lipid bilayer less flowable, if its concentration is too high, it prevents aggregation and crystallization of carbohydrate chains. C connects with Pl in erythrocyte's membrane, sediments in a form of cholesterol clusters between sheets of membrane and can cause disorder in function of receptors and enzymes. Increasing of C concentration assists to applanation of discoid form and spherulation of erythrocytes [15, pp. 587–602, 18, pp. 8–19, 19, pp. 17–38].

Mature erythrocytes are not able to synthesize proteins and lipids, sustenance and changes of their maintenance and correlation are derived from microenvironment of erythrocytes, particularly, from composition of blood plasm, which significantly changes in pathology, what effects morphology of cell, lipid-protein interactions in erythrocyte's membrane and, conditioned by all of the above, activity of enzyme systems [14, pp. 334–354, 15, pp. 587–602, 20, pp. 33–42, 21, pp. 51–53].

Mostly the data obtained in CE coincides with analogical changes of protein-lipid spectrum of erythrocyte's membrane, discovered in other types of pathology [22, pp. 64–69, 23, pp. 5–87, 24, pp. 17–22, 25, pp. 296–300]. As for this, we have assumptions about existence of biological expediency of evolutionally fixed response of proteins and lipids to pathological influences. Existence of a single-type reaction can be caused by the start of universal answer on external action, which is apparently based on physical-chemical system of regulation of immune homeostasis and LP, what function on all of the levels of biological system's organization. As far as processes of LP are connected to the most important physical-chemical properties of membranes (penetrability, viscosity, phase condition), so the development of different pathologies accompanies by molecular changes of cell's plasmatic membranes. Membranes of erythrocytes are ones of the most sensitive, they can change their composition quite fast even in conditions of normal organism functioning. Compensatory changes in protein-lipid spectrum of erythrocytes are targeted to maintenance of crystalline liquid structure of membrane, barrier, receptor, absorption, transport and other properties and penetrability of membrane. Uniformity of adaptive biochemical reactions on protein and lipid level is, obviously, one of the most ways of evolution of living beings, what contribute absence of qualitative differences in response of organism to influence of external factors. However, in connection with unequal sensibility of physical-chemical system of LP regulation parameters and their recovering ability, magnitude and character of interconnections between tightly coordinated indices in norm can significantly differ not only in

dependence from nature and intensity of external factor, but also from initial physiological condition of biological system, what determines that qualitative differences, discovered not only in various researches, but also depend on the time of exposure [12, pp. 7–27, 14, pp. 334–354, 15, pp. 587–602, 26, pp. 3–40, 27, c. 53–65].

Conclusion

Changes of maintenance and correlation of lipid composition of membrane we've established, first of all, lowering in maintenance of membrane GPL and SM, what compose the base of double lipid carcass of cellular membrane and play main role in ordering of protein macromolecules and normal metabolism of erythrocytes along with change of protein's architectonic, leading to serious damages in functional properties of peripheral blood erythrocytes even on early stages of CE, as evinced by increasing of LP processes and maintenance of stable nitrogen oxide metabolites, which is an indirect indicator of NO level. Besides, significant lowering in activity of key enzymes of antioxidant defense (SOD and catalase) evidences about development of endoglobular oxidative stress.

References

1. Eckert L.O., Hawes S.E. Endometritis: The clinical-pathologic syndrome. *Am J Obstet Gynecol,* 2002, no. 690, 5 p.
2. Gombolevskaja N.A., Murav'eva V.V., Marchenko A.A., Ankrikskaja A.S. *Akusherstvo i ginekologija*. 2012. № 8, pp. 40–45.
3. Sharkey A.M., Smith S.K. The endometrium as a cause of implantation failure. *Best Pratice Research Clinical Obstetrics Gynecology,* 2003, vol. 17, no. 2, pp. 289–307.
4. Kulakov V.I., Shurshalina A.V. Khronicheskiy endometrit kak prichina narusheniya reproduktivnoy funktsii. *Ginekologiya*, 2012, vol. 14, no. 4, pp. 16–18.
5. Konoplya A.A., Karaulov A.V., Konoplya A.I., Gavrilyuk V.P. *Vzaimosvyaz' korrektsii immunnykh i oksidantnykh narusheniy so strukturno-funktsional'nymi svoystvami eritrotsitov pri khronicheskikh* [Correla-

tion of the correction of immune and oxidant disorders with the structural and functional properties of erythrocytes in chronic salpingo-oophoritis]. Kursk: Izd-vo GOU VPO KGMU Roszdrava, 2009, pp. 5–36.

6. Togaybaev A.A, Kurguzkin A.V., Rikun I.V. *Laboratornoe delo*, 1988, no. 9, pp. 22–24.
7. Semko G.A. *Ukrainskiy biokhimicheskiy zhurnal*, 1998, no. 70, pp. 113–118.
8. Dodge G.T., Mitchell C., Hanahan D.J. The preparation and chemical characteristics of hemoglobin free ghosts of human eryrhrocytes. *Arch. Biochem. Biophys*, 1963, no. 100, pp. 119–130.
9. Krylov V.I., Vinogradov A.F., Efremova S.I. Metod tonkosloynoy khromatografii lipidov membran eritrotsitov. *Lab. Delo*, 1984, no. 4, pp. 205–206.
10. Laemli U.K. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature*, 1970, no. 227, p. 680.
11. Smith J.E. Erythrocyte membrane structure, function and pathophysiology. *Vet. Pathol*, 1987, vol. 24, no. 6, pp. 471–476.
12. Konoplya A.I., Prokopenko L.G., Dolgareva S.A., Loktionov A.L., Konoplya A.A., Gavrilyuk V.P. *Strukturno-funktsional'nye svoystva eritrotsitov v norme i pri patologii* [Structural and functional properties of erythrocytes in norm and in pathology]. Kursk: Izd-vo KGMU, 2011. pp. 7–27.
13. Shul'ginova A.A., Laskov V.B., Konoplja A.I., Karaulov A.V. *Eksperemental'naja i klinicheskaja farmakologija*. 2016. V. 79, № 7, pp. 3–7.
14. Borovskaya M.K., Kuznetsova E.E., Gorokhova V.G., Koryakina L.B., Kuril'skaya T.E., Pivovarov Yu.I *Byulleten' VSNTs SO RAMN*, 2010, vol. 3, no. 73, pp. 334–354.
15. Shishkina L.N., Shevchenko O.G. *Uspekhi sovremennoy biologii,* 2010, vol. 130, no. 6, pp. 587–602.
16. Shvets V.I., Stepanov A.E., Krylova V.N., Gulok P.V. *Mioinozit i fosfoinozitidy* [Myoinositol and phosphoinositides]. M.: Nauka, 1987, pp. 97–118.
17. Bryzgalova N.Yu., Brazhe N.A., Yusipovich A.I. *Biofizika*, 2009, vol. 54, no. 3, pp. 442–447.
18. Brovkina I.L., Bystrova N.A., Lazarenko V.A., Prokopenko L.G. *Vitaminy. Eritrotsity. Immunitet* [Vitamins. Erythrocytes. Immunity]. Kursk: KGMU, 2013, pp. 8–19.

19. Petrov A.M., Zefirov A.L. Kholesterin i lipidnye plotiki biologicheskikh membran. Rol' v sekretsii, retseptsii i funktsionirovanii ionnykh kanalov. *Uspekhi fiziologicheskikh nauk*, 2013, vol. 44, no. 1, pp. 17–38.
20. Van-Gelder J., Nair C., Dhall D. Erythrocyte aggregacion and erythrocyte deformability modify the permeability of erythrocyte enriched fibrin network. *Throm*. *Res.,* 1996, vol. 82, no. 1, pp. 33–42.
21. Kushnarenko N.N., Govorin A.V., Shcherbakova O.A. *Klinicheskaya meditsina*, 2012, no. 11, pp. 51–53.
22. Budyakov S.V., Konoplya N.A., Gavrilyuk V.P., Konoplya A.I. *Chelovek i ego zdorov'e*, 2010, no. 3, pp. 64–69.
23. Shatokhin M.N., Konoplya A.I., Teodorovich O.V., Gavrilyuk V.P. *Immunometabolicheskiy status i eritrotsity pri patologii predstatel'noy zhelezy; korrektsiya narusheniy* [Immunometabolic status and erythrocytes in the pathology of the prostate; Correction of violations]. M.: Izd-vo GOU VPO KGMU Minzdravsotsrazvitiya Rossii, 2012, pp. 5–87.
24. Konoplya A.I., Shul'ginova A.A. *Patologicheskaya fiziologiya i eksperimental'naya terapiya,* 2016, vol. 60, no. 1, pp. 17–22.
25. Sumin S.A., Avdeeva N.N., Bystrova N.A., Konoplya A.I., Komissinskaya L.S. *Anesteziologiya i reanimatologiya,* 2016, vol. 61, no. 4, pp. 296–300.
26. Prokopenko L.G., Brovkina I.L., Konoplya A.I. *Okislitel'nyy stress* [Oxidative stress]. Kursk: Izd-vo GOU VPO KGMU Roszdrava, 2008. 68 p.
27. Ryazantseva N.V., Novitskiy V.V. *Uspekhi fiziologicheskikh nauk*, 2004, vol. 1, no. 1, pp. 53–65.

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