

gested carbohydrates. No significant difference between the indices of triglyceride level in the alveolar bone and the gum tissue in the 3rd group animals was found ($P_{3,1} \geq 0,01-0,05$) compared to the corresponding indices in the 1st group animals. Conclusions. The level of triglycerides in the periodontal tissues of the experimental animals depends on the food ration. When keeping animals on unbalanced vegetable fat ration the signs of insulin resistance in the periodontal tissues are detected to be increased. The unbalanced animal fat ration does not affect the studied tissues.

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FEATURES OF HUMORAL REGULATION MECHANISM OF IRON DELIVERY TO THE BONE MARROW IN CONDITION OF HYPOXIC HYPOXIA ACTION

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Iron is necessary to each organism. Ability of this transition metal exists in two redox conditions makes it useful in catalytic center of the primary biochemical reactions. DNA synthesis, transporting of oxygen and electrons and respiration require the iron. The same qualities, that make the iron useful in each of these reactions, make it toxic. Free iron has the ability to generate the oxidative radicals that damage the main biological compounds such as lipids, proteins and DNA. Humans iron metabolism is characterized by regulation of reabsorption and excretion of iron's quantity. Inadequate responses or the absence of responses lead to anemia or iron overload. Until that time, the mechanism and regulatory factors that provide process of iron metabolism regulation in organism and sufficient delivery of iron to the bone marrow for synthetic processes, is not clearly established. The question about realization of feedback between hematopoiesis in the bone marrow and iron delivery system for providing adequate synthesis of hemoglobin by erythroid elements remains one of the unsolved problems of classic hematology. Object. To determine the influence of thin humoral factors of iron metabolism in rats after hypoxic hypoxia action. Methods. Studies were done on 166 white laboratory male rats. Animals were divided into 5 groups: the 1st group – intact rats (I); the 2nd group – the rats – donors of blood serum (D), were placed into the hypoxia chamber and undergo of hypoxic hypoxia action during 18 hours, barometric and oxygen partial pressure in the hypoxia chamber corresponded with notional "height" to 4,000 meters above sea level; the 3rd group – rats-recipients 1 of blood serum (R1), which were introduced intramuscularly 2 ml of blood serum of the 2nd animals group; the 4th group – rats-recipients 2 (R2), which were introduced intramuscularly 2 ml of blood serum of the 3rd animals group; the 5th group – control (C), animals were placed into the hypoxia chamber without changes of barometric and partial pressure and were introduced intramuscularly 2 ml of physiological solution. To determine the influence of thin humoral factors of iron metabolism in rats after hypoxic hypoxia action the whole blood and serum were studied. Laboratory clinical tests, biochemical and statistical methods to determine reticulocytes, erythrocytes, hemoglobin quantity and hematocrit, indicators of iron serum, total iron binding capacity (TIBC) and unsaturated iron binding capacity (UIBC) were used. Results. On the 1st day after 18 hours of the animals' staying under hypoxic hypoxia conditions the increase quantity of reticulocytes were detected. The indicators of blood serum iron transport were decreased except indicators of UIBC. In the studies of animals – recipients 1, with erythropoietin' absence in their blood serum, were determined that in the group of animals – recipients 2 indicators of total iron and transferrin saturation were twice bigger in comparison with control group. On the 5th day, the indicators of total iron and transferrin saturation were decreased relatively to the 3rd day, but were increased relatively to the control group. On the 7th day total iron, TIBC, UIBC and transferrin saturation return to norm and did not differ in all groups. Conclusions. Thus, during activation of erythropoiesis the increasing delivery of iron to the bone marrow is not stimulated by erythropoietin. Researches showed, that under the action of this hormone the conditional factor of a thin humoral regulation is participating in one of the stages of stimulation of iron mobilization was formed.

Key words: erythrocytes, reticulocytes, iron, anoxia, rats.

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Introduction

Iron is essential for living organisms. This transition of the metal exists in two redox conditions, which make it useful in catalytic center of the primary biochemical reactions. DNA synthesis, transporting of oxygen and electrons, and respiration require the iron. The same qualities, that make the iron useful in each of these reactions, make it toxic. Free iron has the ability to generate the oxidative radicals that

damage the main biological compounds such as lipids, proteins and DNA. Human body iron metabolism is characterized by balance between re-absorption and excretion of iron quantity. Inadequate responses or their absence lead to anemia or iron overload [8]. Recently, much attention of physiologists, pathophysiologists and clinicians has been paid to the issue on iron homeostasis regulation that is an important process for normal organism functioning. Iron

metabolic disorders, its deficiency or excessive amount determine a pathogenesis of most diseases [2]. Iron regulation disorders, whether they are hereditary or acquired, lead to iron deficiency in organism and can cause severe diseases. Shortage of iron due to poor dietary intake results in iron deficiency anemia (IDA) [7,9], and this problem remains urgent for medicine despite great progress in diagnosis and treatment of IDA. Activity of all proteins that participate in iron metabolism is strictly regulated that enables to maintain iron homeostasis [1]. Nevertheless, the mechanism and regulatory factors that provide iron metabolism regulation in organism and sufficient iron delivery to the bone marrow for synthetic processes, is still unclear. The question about realization of feedback between bone marrow hematopoiesis and iron delivery system for providing adequate synthesis of hemoglobin by erythroid elements remains one of the unsolved problems of classic hematology.

Object: to determine the influence of fine humoral factors of iron metabolism in rats exposed to hypoxic hypoxia.

Materials and methods

Studies were carried out on 166 white laboratory male rats. Animals were divided into 5 groups: the 1st group involved intact rats (I). The 2^d group included rats who were donors of blood serum (D). They were placed into the hypoxia chamber and underwent hypoxic hypoxia during 18 hours, barometric and oxygen partial pressure in the hypoxia chamber corresponded to notional "height" of 4000 meters above sea level. The 3rd group involved rats-recipients 1 of blood serum (R1), who were administered 2 ml of blood serum taken from the animals of the 2^d group, intramuscularly; the 4th group included rats-recipients 2 (R2), who were introduced intramuscularly 2 ml of blood serum taken from the animals of the 3rd group; the 5th group was control (C) and made up of animals placed into the hypoxia chamber without changes of barometric and partial pressure. These animals were introduced 2 ml of physiological solution intramuscularly. Keeping the animals and their involving into experiments were carried out according to the regulations of European convention on the protection of vertebrata, which are used for experimental and other scientific purposes (Strasbourg, 18.03.86), the law of Ukraine "Animal Protection from Cruel Appeal" (№ 1759 from 15.09.2009). The killing and further taking the material from the animals of the 2^d, 3rd, 5th groups were done on the 1st and 3rd days after exposure to hypoxia, and in animals of 4th group on the 3rd, 5th, 7th days. The parameters we evaluated in the study were the following: the reticulocytes quantity by the standard kit ReticuloFarb "Filisit" (Ukraine); the red blood cells (RBC), hemoglobin amount and hematocrit were

assayed by the haematology analyzer MYTHIC 18 (France); iron serum was assessed by the kit Zalizo Prestige 24i "CORMEY" (Poland); total iron binding capacity (TIBC), unsaturated iron binding capacity (UIBC), percentage of transferrin saturation (TS) were evaluated by the kit Zalizo v'yazuyuchya zdatnist' Prestige 24i "CORMEY" (Poland) in an automatic biochemical analyzer PRESTIGE 24i (Japan). Processing of the obtained numerical results was conducted through statistical methods - STATISTICA® for Windows 6.1 (StatSoft Inc., № AXXR712D833214FAN5). The difference between the variables was considered statistically significant at the $p \leq 0,05$.

Results

On the 1st day after hypoxia chamber action the amount of erythrocytes, hemoglobin, hematocrit and blood serum unsaturated iron - binding capacity in the donors of experimental group animals did not differ from the findings demonstrated by the animals of intact and control groups (**tabl. 1**). The reticulocytes were significantly increased ($26,1 \pm 2,2$) compared with the 1st and 5th groups ($18,2 \pm 0,7$; $18,4 \pm 0,8$ accordingly). Indicators of serum iron ($24,2 \pm 0,9$), blood serum total iron binding capacity ($44,3 \pm 1,1$) and percentage of transferrin saturation ($55,7 \pm 2,7$) were significantly decreased compared with intact and control groups (**tabl. 1**). During the experiment the indices of peripheral blood and blood serum iron - transport function in the animals of intact group did not significantly differ from the indices in the control group (**tabl. 1**). On the 3rd day after hypoxic hypoxia action, in animals of the 2^d experimental group the erythrocytes, hemoglobin and hematocrit indicators did not differ from those indices in the 1st and 5th groups (**tabl. 1**). The reticulocytes were significantly increased ($41,1 \pm 0,7$) compared with rats on the 1st day in the 2^d experimental group ($26,1 \pm 0,9$) and intact group ($18,2 \pm 0,7$). In rats of the 2^d experimental group the total blood serum of iron was increased ($44,6 \pm 1,2$) in comparison with intact group - ($32,4 \pm 0,9$). Blood serum TIBC of experimental animals significantly higher ($79,3 \pm 1,8$) than indicators of intact group ($47,6 \pm 1$; $p \leq 0,05$). Blood serum UIBC of the 2^d experimental group greatly increased ($31,2 \pm 1,4$) relatively to the control ($15,1 \pm 1$). Transferrin saturation indicator of experimental group is less ($52,3 \pm 2,8$) than control indicators ($68,2 \pm 2,2$). On the 1st day after injection of animals - donors' blood serum in rats' recipients 1 the reticulocytes quantity is significantly increased ($39,1 \pm 0,6$) in comparison with control and intact groups ($18,7 \pm 0,7$; $18,2 \pm 0,7$). Hematocrit and quantity indicators of erythrocytes and hemoglobin do not differ from the same parameters of the 1st and 5th groups (**tabl. 2**).

Table 1
Indicators of rats (donors) peripheral blood and iron-transport function (n=6)

	Intact	Control		Experiment	
		1 day	3 day	1 day	3 day
Reticulocytes (‰)	18,2±0,7	18,4±0,8	17,6±0,6	26,1±0,9 [⊠]	41,1±0,7 [⊠]
Erythrocytes (x10 ¹² /L)	7,74±0,4	7,76±0,5	7,74±0,5	7,64±0,4	7,65±0,5
Hemoglobin (g/L)	156,1±8,7	155,4±8,7	156,2±8,1	155,3±7,9	155,8±8,4
Hematocrit (%)	43,2±0,8	42,7±0,8	42,2±0,7	43,1±0,9	42,9±0,8
Iron (µM/L)	32,4±0,9	33,4±0,7	33,7±0,8	24,2±0,9	44,6±1,2 [⊠]
TIBC (µM/L)	47,6±1	48,2±0,9	48,1±0,8	44,3±1,1 [⊠]	79,3±1,8 [⊠]
UIBC (µM/L)	15,2±0,8	15,0±0,9	15,1±1	21,1±0,8	31,2±1,4 [⊠]
TS (%)	68,6±2,6	67,1±2,1	68,2±2,2	55,7±2,7 [⊠]	52,3±2,8 [⊠]

Notes: [⊠] - the result is significant in comparison with intact group, (p<0,05);

[⊠] - the result is significant in comparison with previously observations term's (p<0,05).

Relatively the total iron indicators (32,4±0,9; 32,7±1,1), TIBC (47,6±1,1; 47,2±1,2), UIBC (15,2±0,3; 15,3±0,8), transferrin saturation percent (68,6±2,6; 67,9±2,2) of intact and control

groups accordingly, total iron indicators (44,9±1,6), TIBC (63,3±1,9), UIBC (20,4±1,7), transferrin saturation percent (71,2±2,2) of the 3rd experimental group is significantly increases.

Table 2
Peripheral blood and iron-transport function indicators in rats – recipients 1 of experimental group after injection of animals – donors' blood serum (n=6)

	Intact	Control Recipients 1	Experimental Recipients 1
Reticulocytes (‰)	18,2±0,7	17,7±0,7 [⊠]	39,1±0,6 [⊠]
Erythrocytes (x10 ¹² /L)	7,74±0,4	7,76±0,4	7,65±0,6
Hemoglobin (g/L)	156,1±8,7	156,2±8,5	156,4±8,6
Hematocrit (%)	43,2±0,8	43,1±0,7	42,5±0,6
Iron (µM/L)	32,4±0,9	32,7±1	44,9±1,6 [⊠]
TIBC (µM/L)	47,6±1	47,2±1,2	63,3±1,9 [⊠]
UIBC (µM/L)	15,2±0,8	15,3±0,8	20,4±1,7 [⊠]
TS (%)	68,6±2,6	67,9±2,2	71,2±2,2 [⊠]

Notes: [⊠] - result is significant in comparison with intact group, (p<0,05).

Peripheral blood and iron transport function indicators in recipients from the 1st till 7th days do not differ from indicators of intact group (tabl. 3) that is why hereinafter these terms will not cite. Hematocrit and the reticulocytes, erythrocytes and hemoglobin quantity in recipients of experimental group during seven days remain unchanged compared control group (tabl. 3) and will not be compared further. On the first day after injection of group recipients 1 blood serum in recipients 2 of experimental group detected the increase indicators of total iron (46,7 ±0,4), TIBC (66,4±0,6), UIBC (19,7±0,7), transferrin saturation (70,7±2,8) relatively to intact group (32,4±0,9; 47,6±1; 15,2±0,8; 68,6±2,6 accordingly).

On the third day the indicators of total iron

(79,2±0,8), TIBC (110,2±0,8), UIBC (42,0±2,2), transferrin saturation (79,0±2,7) continued to increase relatively the 1st experiment day (Tab. 3) and in comparison with control rats group (31,7±0,8; 48,3±0,9; 15,3±0,9; 68,7±2,4).

On the fifth day it was determined the decrease of indicators of total iron (46,8±0,7), TIBC (67,3±0,6), UIBC (22,4±2,1), transferrin saturation (68,6±2,4) relatively the 3rd day (tabl. 3), but they increased relatively to control group (32,4±0,9; 47,3±0,7; 14,7±0,7; 67,9±2,8).

On the seventh day total iron (32,6±0,8) TIBC (48,0,2±0,6), UIBC (15,3±0,7), transferrin saturation (67,2±2,3) returned to the norm relatively to intact and control groups.

Table 3
Peripheral blood and iron-transport function indicators in rats – recipients 2 of experimental group after injection of animals – recipients'1 blood serum (n=6)

	Intact	Control Recipients 2				Experimental Recipients 2			
		1day	3 day	5 day	7 day	1 day	3 day	5 day	7 day
Reticulocytes (‰)	18,2±0,7	18,4±0,7	18,1±0,8	17,8±0,8	18,3±0,6	18,3±0,8	19,2±0,7	18,6±0,7	18,3±0,8
Erythrocytes (x10 ¹² /L)	7,74±0,4	7,26±0,9	7,44±0,6	7,91±0,8	7,56±0,6	7,61±0,7	7,67±0,9	7,56±0,7	7,46±0,8
Hemoglobin (g/L)	156,1±8,7	158±8,8	157±9,1	156,8,9	154±8,7	157,8±9,2	156,6±9,7	158,2±8,6	155,4±8,9
Hematocrit (%)	43,2±0,8	42,6±0,8	42,9±0,9	42,4±0,7	44±0,8	42,7±0,9	42,3±0,7	43,2±0,6	42,1±0,8
Iron (µM/L)	32,4±0,9	32,8±1	31,7±0,8	32,4±0,9	32,7±0,7	46,7±0,4	79,2±0,8	46,8±0,7	32,6±0,8
TIBC (µM/L)	47,6±1	48,2±0,7	48,3±0,9	47,3±0,7	48,4±0,8	66,4±0,6 [⊠]	110,2±0,8 [⊠]	67,3±0,6 [⊠]	48,0±0,6 [⊠]
UIBC (µM/L)	15,2±0,8	15,4±0,8	15,3±0,9	14,7±0,7	15,7±0,8	19,7±0,7 [⊠]	42,0±2,2 [⊠]	22,4±2,1 [⊠]	15,3±0,7 [⊠]
TS (%)	68,6±2,6	68,1±2,2	68,7±2,4	67,9±2,8	67,5±2,7	70,7±2,8 [⊠]	79,0±2,7 [⊠]	68,6±2,4 [⊠]	67,2±2,3 [⊠]

Notes: [⊠] - result is significant compared intact group, (p<0,05);

[⊠] - result is significant compared previously observations term, (p<0,05).

Discussion

Humans possess elegant control mechanisms to maintain iron homeostasis by coordinately regulating iron absorption, iron recycling, and mobilization of stored iron. Dietary iron absorption is regulated locally by hypoxia inducible factor (HIF) signaling and iron-regulatory proteins (IRPs) in enterocytes and systematically by hepatic hepcidin, the central iron regulatory hormone [13]. Moreover, the modeling of hypobaric hypoxia plus ferrous sulfate (FeSO₄) effectively alleviated weight loss and intestinal mucosa damage induced by hypobaric hypoxia, whereas FeSO₄ aggravated hypobaric hypoxia-induced weight loss, liver enlargement, spleen atrophy, and intestinal damage [12]. The iron biomarkers study in conditions of acute hypoxia after exercise showed that the level of serum ferritin and transferrin significantly were increased immediately in post-exercise conditions, but returned to baseline 3 hour later [6]. The research of a transport and metabolism adaptation under hypoxia in mountaineers determined that under hypoxemic conditions, the hepcidin function is repressed and duodenal iron transport was rapidly up-regulated. These changes may increase dietary iron uptake and allow release of stored iron to ensure a sufficient iron supply for hypoxia-induced compensatory erythropoiesis [5].

It was determined the erythropoiesis stimulation that confirmed the increase quantity of blood reticulocytes at the first day, after 18 hours staying of animals in conditions of hypoxic hypoxia. In response to said conditions, the erythropoietin was appeared in the blood, after stimulation of the erythropoiesis [3]. The indicators of transport iron in the blood serum were decreased (exception was the indicator UIBC) due to the stimulation of hematopoiesis requires more iron's quantity from the blood serum, but the increase of its absorption gets behind the needs. The absorption's increase leads to appearance in the small intestine of the new microvilli, which updated in a two days [4]. Already, at the third day after hypoxia modeling, the transport iron blood serum increasing, a reticulocytes concentration returned to normal, such as animals' blood serum with stimulated erythropoiesis obtained on the third day, after staying in a hypoxia chamber did not contain the erythropoietin (T_{1/2} of erythropoietin is a half of an hour) [11].

It is considered that stimulation of an iron absorption and reutilization connecting with the hepcidin' level under influence of formed during hypoxia or induced by hypoxia factor (HIF), or by stimulant erythropoiesis – erythropoietin [10]. For checking this hypothesis, we studied the influence of animals – recipient 1 serum, which was erythropoietin – free. Findings at the group of recipient 2 showed, that during erythropoiesis activating the increasing delivery of iron to the

bone marrow is not stimulated by erythropoietin. Possibly, under the action of this hormone the conditional factor of a thin humoral regulation of the iron metabolism was formed to stimulate the iron mobilization.

Conclusions and perspective

During the activation of erythropoiesis the increasing iron delivery to the bone marrow is not stimulated by erythropoietin. Researches show that under the action of this hormone the conditional factor of fine humoral regulation is formed participating in one of the stages of stimulation of iron mobilization.

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Реферат

ОСОБЛИВОСТІ ГУМОРАЛЬНОЇ РЕГУЛЯЦІЇ МЕХАНІЗМІВ ДОСТАВКИ ЗАЛІЗА ДО КІСТКОВОГО МОЗКУ ЗА УМОВ ДІЇ ГІПОКСИЧНОЇ ГІПОКСІЇ

Філімонов В.І., Бурега І.Ю.

Ключові слова: еритроцит, ретикулоцит, залізо, гіпоксія, щури.

Метою роботи стало вивчення особливостей гуморальної регуляції механізмів доставки заліза в кістковий мозок в умовах дії гіпоксичної гіпоксії. Під час активації еритропоезу збільшення доставки заліза в кістковий мозок не стимулюється еритропоетином. Дослідження показали, що під дією цього гормону утворюється якийсь умовний фактор тонкої гуморальної регуляції, який впливає на метаболізм заліза, збільшуючи його рівень в сироватці крові.

Реферат

ОСОБЕННОСТИ ГУМОРАЛЬНОЙ РЕГУЛЯЦИИ МЕХАНИЗМОВ ДОСТАВКИ ЖЕЛЕЗА В КОСТНЫЙ МОЗГ В УСЛОВИЯХ ДЕЙСТВИЯ ГИПОКСИЧЕСКОЙ ГИПОКСИИ

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Ключевые слова: эритроцит, ретикулоцит, железо, гипоксия, крысы.

Целью работы явилось изучение особенностей гуморальной регуляции механизмов доставки железа в костный мозг в условиях действия гипоксической гипоксии. Во время активации эритропоеза увеличение доставки железа в костный мозг не стимулируется эритропоетином. Исследования показали, что под действием этого гормона образуется некий условный фактор тонкой гуморальной регуляции, который влияет на метаболизм железа, увеличивая его уровень в сыворотке крови.

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УЛЬТРАСТРУКТУРНІ ЗМІНИ ТРАВМОВАНОГО СІДНИЧНОГО НЕРВА ЩУРІВ НА ТЛІ РТУТНОЇ ІНТОКСИКАЦІЇ ТА ЇЇ ФАРМАКОЛОГІЧНОЇ КОРЕКЦІЇ

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Нагальним залишається вивчення впливу фармакологічних препаратів які б покращили механізми регенерації периферійних нервів з урахуванням трофічних факторів. Метою даного дослідження було проведення порівняльного ультраструктурного аналізу периферійного нерва щурів за умов мікромеркуріалізму із застосуванням антиоксидантного препарату та без фармакотерапії. В дослідках на білих щурах, які були розподілені на дві групи, відтворили експериментальну модель травми сідничного нерва за умов мікромеркуріалізму. У післяопераційному періоді щурам першої групи фармакотерапію не проводили, в другій групі тваринам внутрішньоочередово вводили щоденно протягом 2 тижнів розчин тіотриазоліну. Досліджували ультраструктурну організацію та морфометричну характеристику дистального відрізка сідничного нерва через 6 та 12 тижнів після пошкодження. Проведене дослідження свідчить, що у групи тварин, яким проводили фармакологічну корекцію тіотриазоліном, активується процес регенерації нерва за умов його пошкодження.

Ключові слова: мікромеркуріалізм, сідничний нерв, регенерація, тіотриазолін.

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Вступ

Україна стала однією із найбільш екологічно забруднених країн на планеті. У регіонах екологічної кризи важкі метали знаходяться як в об'єктах довкілля, так і безпосередньо в організмі людини у дуже високих концентраціях, які

часто перевищують гігієнічний норматив [1, 2]. На фоні погіршення екологічного стану проблема відновлення порушень периферійної інервації, викликаной травмами, не завжди призводить до задовільних результатів. Це пояснюється недостатністю фундаментальних