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Optimising the effect of activated carbon on the microrheological properties of erythrocyte in rats with experimentally developed obesity

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ABSTRACT

Background: Remains not fully clear the impact of intestinal chelators on microrheological violation of red blood cells during the early stages of obesity. It dictates the necessity of experimental investigations' fulfilment on laboratory animals with just developed obesity in them.

Method: Ninety-four of healthy male-rats of Vistar line at the age of 2.5-3 months took into investigation. Twenty-nine animals of them had experienced no impacts and composed the control group. In 65 rats after their putting into small cages (one specimen - in a cage) during 30 days there was developed OB as the result of giving them of high-caloric diet from combined feed (47%), sweet condensed milk (44%), vegetable oil (8%) and vegetable starch (1%). Of the 35 rats received a day for 60 days of activated carbon 25 mg/kg into a stomach. There used biochemical, haematological and statistical methods of investigation.

Results: At obesity development in rats, there found a steady decrease of erythrocytes-discocytes quantity in blood. It accompanied by increase of reversibly and irreversibly changed erythrocytes' quantity in examined animals' blood. At obesity development in rats there was found quick rise of erythrocytes' sum in aggregate and these aggregates' quantity at lowering of free erythrocytes' number. During experimental obesity modelling we noticed very early in rats' blood decrease of erythrocytes-discocytes' quantity, level rise of their reversibly and irreversibly varieties with strengthening of their aggregative ability. It takes place in the background of weakening of erythrocytes' antioxidant protection and activation of lipids' peroxidation in them.

Conclusion: Application of activated carbons capable of rats with experimental obesity resolve arisen they breach microrheological properties of erythrocytes. It is clear that in obesity treatment regimens must be intestinal chelators, capable of positively affect many broken with this pathology haematological indices.

Keywords: rats, erythrocytes, microrheological features, experiment, obesity, activated charcoal

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INTRODUCTION

Now essential medicine is actively exploring mechanisms for the early stages of development of Pathology, using many experimental animal models[1-4] with the obligatory light effects studied pathology.[5] Taking into consideration fundamental significance for a body's vital activity provision of functional and rheological features of essential regular blood elements[6-8] and especially their most numerous population - erythrocytes[9,10] at different diseases[10,11] including very widespread in developed countries cardio-vascular pathology, researchers pay great attention to them.[12,13,14] As a severe basis for this pathology, we consider now obesity (OB) which having genetic[15,16] and behavioural component[17] causes metabolic abnormalities in the whole body [18,19] promoting sometimes firm invalidation of a person in the nearest future.[20] It caused by the fact that developing in a patient's body dysfunctions lead to activation of neutrophils,[21] platelets[22] and change microrheological peculiarities of erythrocytes[23] worsening metabolism in all the tissue.s[24-26] However, the state of erythrocytes' microrheological characteristics at early stages of OB development is not yet studied well enough. Complexity in finding of the earliest stages of erythrocytes' microrheological abnormalities in a human being with initial signs of obesity connected with these persons' fall out of clinicians' field

of view.[27,28] It dictates the need for conducting experimental investigations on laboratory animals with modelling of this pathology development in them.[29,30] Conducting of such experiments will allow to trace the dynamics of the body's normal state[31] in tight connection with early haemostatic and hemorheological[32] and also early vascular dysfunctions.[33,34] Besides, conducting experimental investigations on obesity models can help in working out of rational and practical approaches for early removal of initial rheological abnormalities and activation of hemostasis system.[35,36]

It remains not entirely clear the impact of intestinal chelators on microrheological properties of red blood cells during the development of OB. This information is beneficial for future clinical studies aimed at clarifying pathogenesis justified since the beginning of the rehabilitative effects and their nature with the emerging OB.

In this study, we estimated dynamics of development obesity experimental in early changes of erythrocytes' microrheological features by application of activated carbon.

MATERIALS AND METHODS

All the investigations in the present work were conducted in full correspondence with ethical norms and recommendations on the humanization of work with laboratory animals containing "The European Convent on the protection of vertebrate animals used for experiments or in other scientific purposes" (Strasbourg, 1986).

We took into investigation 94 healthy male-rats of Vistar line at the age of 2.5-3 months received from healthy females by the first-second farrow. Animals' body mass at the moment of taking them into investigation composed 212.4±0.42 gr and their abdominal circumference – 13.8±0.25 cm. Before the investigation all the rats had not participated in any experiments and had suffered no diseases. Twenty-nine animals of them experienced no impacts and composed control group of healthy rats.

In 65 rats after their putting into small cages (one specimen - in a cage) during 30 days there was developed OB as the result of giving them of high-caloric diet from combined feed (47%), sweet condensed milk (44%), vegetable oil (8%) and vegetable starch (1%).[38] Given model allows modelling in maximal degree all the obesity peculiarities relevant to a human being.[39] These rats were randomly divided into the experimental group (35 rats) and control unit the sick rats. Rats pilot group within the next 60 days, the day got into a stomach 25 mg/kg activated charcoal (Asfarma, Russia).

The level of lipids' peroxidation (LPO) in animals' plasma was found according to the quantity of thiobarbituric-acid (TBA)-active products in it with the help of a set "Agat-Med" and according to the content of acylhydroperoxides (AHP)[40] taking into consideration the level of antioxidant activity (AOA) of blood liquid part.[41] LPO in erythrocytes defined with the help of concentrations in them of malonic dialdehyde (MDA) and AHP [40]. We estimated in them enzymatically the level of healthy cholesterol (CS) by a set "Vitaldiagnostikum" (Russia) and found the concentrations of common phospholipids (CPL) according to phosphorus content with calculation of the ratio CCS/CPL. In erythrocytes we defined the activity of catalase and superoxide dismutase (SOD).[40]

The cytoarchitectonics of red corpuscles defined with light phase-contrast microscopy. All the erythrocytes were subdivided into discocytes, reversibly deformed and irreversibly changed forms.[42] Erythrocytes' aggregative activity was found out with the help of light microscope in Goriajev's box by their aggregates' quantity, quantity of aggregated and not having entered the aggregation red corpuscles in the meal of washed erythrocytes.[43] The results processed by Student's criterion (t).

RESULTS

In the result of obesity model's reproduction, the rats developed stable increase in body mass and bulk of the abdominal cavity (Table 1).

At experimental OB development in rats, we noticed increase of AHP and TBA-active products' quantity in plasma. The number of plasma TBA-products in experimental animals underwent analogical dynamics. Found LPO increase at OB modelling in rats turned out to be possible because of plasma AOA weakening on 18,1% (Table 1). Against the backdrop of activated carbon consumption marked changes in the forecast indicators, approaching the level of healthy control by the end of the observation.

At OB development in experimental rats cholesterol quantity in erythrocytes rose a bit (to 1.06±0.027 mkmol/10^{12}ar.), while the content of CPL in their membranes tended to decrease (to 0.61±0.034 mkmol/10^{12}ar.), what led to a reliable increase of the gradient CS/CPL. Against the backdrop of activated carbon consumption in erythrocytes decreased the amount of CS and CPL increased overall by ensuring through 60 days of observing the normalisation property of morphofunctional ratio of red blood cells.

During OB development, LPO activated in rats' erythrocytes owing to activity weakening of their

Table 1. Dynamics of body weight, biochemical and hematological parameters in experimental rats

Indicators	Experimental formation of pathology, M±m		Corrective effect on rats with formed pathology, M±m, n=35				Control, M±m	
	initial state, n=65	end of pathology modeling, n=65	initial state	20 days	40 days	60 days	sick, n=30	healthy, n=29
body weight, g	112.4±0.42	282.6±0.37 p<0.01	281.9±0.42 p<0.01	270.6±0.56 p<0.01	256.1±0.33 p<0.05	248.9±0.49 p<0.05	284.6±0.58 p<0.01	215.1±0.43
belly girth, cm	13.8±0.25	16.8±0.29 p<0.01	17.0±0.31 p<0.01	16.2±0.37 p<0.01	15.6±0.25 p<0.05	15.3±0.39	17.2±0.46 p<0.01	13.7±0.20
Acylhydroperoxides of plasma, D_{233}/l ml	1.56±0.014	1.90±0.026 p<0.01	1.91±0.036 p<0.01	1.84±0.028 p<0.01	1.72±0.029 p<0.05	1.60±0.024	1.96±0.032 p<0.01	1.63±0.019
Thiobarbituric acid-products of plasma, mkmol/l	3.65±0.026	4.32±0.042 p<0.01	4.22±0.037 p<0.01	4.10±0.039 p<0.01	3.86±0.046 p<0.05	3.70±0.031	4.28±0.041 p<0.01	3.69±0.32
Antioxidant activity of plasma, %	28.7±0.22	24.2±0.40 p<0.01	24.4±0.42 p<0.01	25.6±0.47 p<0.01	26.3±0.30 p<0.05	28.4±0.36	24.0±0.49 p<0.01	28.8±0.29
cholesterol of erythrocytes, mkmol/10^{12} erythrocytes	0.90±0.021	1.06±0.024 p<0.01	1.05±0.026 p<0.01	0.98±0.028 p<0.05	0.94±0.026	0.93±0.024	1.07±0.040 p<0.01	0.92±0.023
common phospholipids of erythrocytes, mkmol/10^{12} erythrocytes	0.66±0.020	0.60±0.030 p<0.01	0,60±0.033 p<0.01	0.63±0.036 p<0.05	0.65±0.027	0.67±0.030	0.60±0.033 p<0.01	0.68±0.022
cholesterol/common phospholipids of erythrocytes	1.36±0.036	1.76±0.042 p<0.01	1.76±0.046 p<0.01	1.55±0.031 p<0.01	1.45±0.025 p<0.05	1.39±0.029	1.55±0.038 p<0.01	1.35±0.019
acylhydroperoxides of erythrocytes, D_{233}/10^{12} erythrocytes	2.70±0.012	3.60±0.019 p<0.01	3.57±0.025 p<0.01	3.29±0.030 p<0.01	3.05±0.026 p<0.05	2.85±0.032	3.55±0.039 p<0.01	2.74±0.017
malonic dialdehyde of erythrocytes, nmol/10^{12} erythrocytes	0.91±0.014	1.15±0.025 p<0.01	1.16±0.026 p<0.01	1.09±0.030 p<0.01	1.02±0.032 p<0.05	0.96±0.019	1.17±0.040 p<0.01	0.91±0.018
catalase of erythrocytes, ME/10^{12} erythrocytes	9890.0±13.2	8720.0±16.7 p<0.01	8710.0±22.6 p<0.01	9020.0±18.6 p<0.01	9310.0±17.6 p<0.05	9920.0±18.5	8735.0±18.4 p<0.01	9880.0±11.9
superoxidismutase of erythrocytes, ME/10^{12} erythrocytes	1810.0±3.10	1620.0±4.20 p<0.01	1610.0±5.46 p<0.01	1680.0±4.40 p<0.01	1720.0±4.75 p<0.05	1810.0±5.17	1590.0±7.10 p<0.01	1830.0±4.05
erythrocytes-discocytes,%	84.0±0.32	71.2±0.41 p<0.01	71.5±0.47 p<0.01	75.2±0.52 p<0.01	78.2±0.46 p<0.05	82.4±0.42	70.5±0.54 p<0.01	84.0±0.34
reversibly modified erythrocytes,%	10.0±0.10	17.3±0.26 p<0.01	17.1±0.23 p<0.01	14.6±0.32 p<0.01	12.2±0.34 p<0.05	10.9±0.23	17.5±0.49 p<0.01	9.5±0.29
irreversibly modified erythrocytes,%	6.0±0.19	11.5±0.24 p<0.01	11.4±0.30 p<0.01	10.2±0.31 p<0.01	9.6±0.24 p<0.01	6.7±0.21	12.0±0.38 p<0.01	6.5±0.25
sum of all the erythrocytes in an aggregate	37.6±0.11	47.5±0.20 p<0.01	47.0±0.16 p<0.01	43.4±0.14 p<0.01	41.2±0.19 p<0.05	38.8±0.10	46.7±0.14 p<0.01	37.3±0.07
quantity of aggregates	8.8±0.09	13.6±0.17 p<0.01	13.4±0.22 p<0.01	10.9±0.15 p<0.01	9.7±0.11 p<0.05	8.9±0.09	12.4±0.10 p<0.01	8.8±0.04
quantity of free erythrocytes	249.1±0.67	222.4±0.73 p<0.01	223.4±0.62 p<0.01	231.0±0.50 p<0.01	239.2±0.42	247.3±0.38	227.3±0.65 p<0.01	249.2±0.52

Conventions: p - found reliability of indices' differences with control group healthy

antioxidant protection (Table 1). With the use of activated charcoal in rats with OB AHP and MDA content in erythrocytes progressively declined and 60 days of the experiment reached a level close to the level of healthy control. The changes revealed activity of LPO in erythrocyte observed animals are possible as a result of the depression in the formation they have OB, and then against the backdrop of activated carbon consumption recovering their activity of catalase and SOD (Table 1). The result achieved is principally provided the correlation Dynamics microrheological properties of erythrocytes.

At OB development in rats, we found a steady decrease of erythrocytes-discocytes quantity in blood which. It was accompanied in blood of experimental animals by corresponding quantity dynamics of changed reversibly and irreversibly erythrocytes, increasing at OB development. At OB development in rats we found sum increase of red corpuscles in aggregate and quantity of these aggregates at simultaneous number lowering of free red corpuscles (Table 1). As a result of the use of entero sorbent in rats with increased OB formed erythrocytes-discocytes and lowering their modified forms to control level of healthy. Against the backdrop of intestinal chelators in rats with shaped OB found reduction of red blood cells in the unit and the number of these units, while increasing the number of free of red blood cells to control healthy animals through 60 days surveillance (Table 1). The absence of intestinal patients controls group rats accompanied by the persistence they have obesity and all violations of the biochemical and haematological characteristics.

DISCUSSION

Even though in the basic of OB development in human population lie not only environmental impacts but also presence of different genetic abnormalities,[44,45] the applied model can consider as quite adequate for the achievement of putting in the work purpose.

In the result of experimental OB development in rats, we created pathological state very near to such one at genetically determined OB.[46,47] At the same time, AOA of blood weakens very fast promoting quantity increase in it of AHP and TBA-products and negatively influencing metabolism in tissues. Besides, activation of LPO processes in liquid part of blood causes alteration of vascular endothelium[48,49] of natural blood elements' outer structures[50,51] including the most numerous their population - erythrocytes, thereby negatively influencing their different functions.[10,11] It is burdened by hypoxia inevitably developing in rats with OB[52] and forming in erythrocytes membranopathy having in its basis increase of CS in them with the tendency to CPL lowering at simultaneous activation in erythrocytes of lipids' peroxidation in the result of their antioxidant protection lowering. Use of entero sorbent has streamlined body mass rats and biochemical indices of their plasma. They have reached the level of healthy rats control.

Forming situation mostly promotes the loss by a part of erythrocytes of standard biconcave form what makes the process of their moving along capillaries intricate.[19] Forming changes in erythrocytes lead to quantity increase in blood of their reversibly and irreversibly changed forms.[22] So, in rats by the moment of OB development in them, the quantity of erythrocytes transformed by echinocytosis into spheres, with the appearance of different forms' acanthas on their surface and stomacytosis to unilaterally arched disk, significantly exceeds the same at the beginning. Further transformation inevitably goes in the direction of spheroechinocyte, spherostomatocyte and, finally, spherocyte which soon must be destroyed.[10] Consumption of rats of activated charcoal has led them to form the bulk of the recovery of red blood cells, which significantly improved microcirculation.

Found in rats with formed OB strengthening of erythrocytes' aggregation has mostly in its basis appearing changes of their membrane's charge because of glycoproteins' degradation on it. They have negative charge on the background of active LPO.[53] Intensification of oxygen active forms' generation in these conditions provides the rats with OB by oxidative alteration of membrane's structures at simultaneous damage of plasma globular proteins able to be connected in the kind of "bridges" between separate erythrocytes and realise the process of their aggregation. Besides, LPO products gradually increase the threshold of erythrocytes' deaggregation on behalf of erythrocytes' adhesion strengthening in aggregates, speed rise of aggregation process between itself and platelets on the background of oxidative damages of their membrane's lipids.[54,55]

It becomes clear that found a very early rise of erythrocytes' aggregation in rats with developing OB mostly connected with the impact of catecholamines, the concentration of which, as it is known, from the first development stages of cardio-vascular pathology and especially OB significantly increases.[56] As the result of α_1-receptors' activation in these conditions as mediator functions the system Ca^{2+}-calmodulin with involvement into the cascade of phosphatidyl inositol's intracellular reactions. Activation of α_2-adrenoreceptors takes place by adenylate cyclase suppression owing to the impact

of a receptor-agonist on Gi-proteins leading to lowering of cAMF quantity in a cell and stimulating Ca^{2+} inflow into a cell[57,58] what additionally rises erythrocytes' aggregation. As a result of the use of activated charcoal in rats with the newly formed OB easing aggregation of red blood cells to the control level of healthy.

Reducing the number of freely moving in the blood of rats with OB treated with activated coal, aggregates leads to preserving endothelial layer of their vessels, while minimising the impact of subendothelial patterns on processes of hemostasis.[54,59] The normalisation of the number of freely circulating units ensures optimum hemocirculation in vasa vasorum, thereby significantly increasing vascular metabolism, contributing to the strengthening of the disaggregates release from endothelial cells.[60,61]

It is clear that even recently developed obesity considered as perilous state connected with the development of metabolic abnormalities complex[62,63] able to worsen headlong erythrocytes' microrheological features and so weaken hemodynamics in capillaries. As shown earlier, such abnormalities can cause evident activation of hemostasis system's components[64,65] significantly increasing the risk of thrombosis coming[66] — all these demands from clinicians to pay more attention to original forms of obesity.

Received the study results have shown the ability to reverse the changes if the newly developed OB. It becomes clear that the return of the mammals on the optimal diet and conducting treatment every other day can lead to gradual spending excess fat deposits without fasting. Developing while optimising microrheological properties of erythrocytes is mostly the basis for optimising the metabolism in the capillaries and healing the entire body. The authors hope their study again will draw the attention of clinicians on the ability of intestinal chelators in the treatment of OB.

CONCLUSION.

During experimental OB modelling in rats' blood, we noticed very early lowering of erythrocytes-discocytes content, raise the level of their reversibly and irreversibly changed variants with strengthening of their aggregative ability. It happens in the background of increase in erythrocytes of cholesterol/common phospholipids' gradient, weakening of their antioxidant protection and activation of lipids' peroxidation in them.

On this reason even brief existence of obesity in a body can lead to the development of metabolic abnormalities' complex able to worsen headlong erythrocytes' microrheological features and, so, break hemodynamics in capillaries. Application of activated carbons capable of rats with experimental obesity resolve arisen they breach microrheological properties of erythrocytes. It is clear that in obesity treatment regimens must be intestinal chelators, capable of positively affect many broken with this pathology haematological indices.

CONFLICT OF INTEREST.

No Conflict of interest to declare.

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