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Physiological Features Of Platelet Aggregation In Aging Mammals Against The Background Of Physical Exertion.

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ABSTRACT

Aging is an inevitable, in many ways genetically conditioned, process of extinction of the body's functions, resulting in its death. Age changes can adversely affect the activity of the mammalian system of platelet hemostasis, often causing a thrombophilic situation in their body. This is of great importance in the pathogenesis of the development and progression of the cardiovascular pathology, which increasingly affects a person with age. It is of great practical interest to carry out experimental work on the search for various options for optimizing platelet activity. As the most accessible and devoid of side effects, physical exercises seem to be the most preferable, which can reduce the severity of platelet activity in cardiovascular disease, and, thereby, reduce the likelihood of thrombosis - an important factor in limiting life expectancy. The goal of the study is to determine the ability of aged rats to contain increased platelet aggregation with age by physical exertion. The study included 26 healthy male rats of 12 months of age who experienced daily physical activity during the year. The control is represented by 91 healthy male colors: 30 animals of 12 months of age, 32 rats of 18 months and 29 animals of 24 months of age. Biochemical, hematological and statistical methods of investigation has been applied. In control rats, as the age increases, there is a gradual increase in platelet aggregation. Regular daily exercise in rats between 12 and 24 months. Life stabilizes the aggregation activity of platelets, inhibiting its increase with age.

Keywords: platelets, aggregation, aging, rats, physical activity.

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INTRODUCTION

Aging is inevitable, in many ways genetically conditioned [1], the process of extinction of the body's functions, resulting in its death [2]. Age changes can adversely affect mammalian activity on the activity of the platelet hemostasis system, causing in their organism often a thrombophilic situation [3, 4]. This is of great importance in the pathogenesis of the development and progression of the cardiovascular pathology, which increasingly affects a person with age [5, 6]. Considering that the surface of activated platelets is the "bridgehead" for all hemostasis processes, which, under the conditions of weakening disaggregation mechanisms, lead to the occlusion of various vessels [7,8], it is of great practical interest to carry out experimental works on searching for various options for optimizing platelet activity. As the most accessible and devoid of side effects, physical exercises seem to be the most preferable, capable of decreasing the platelet activity in cardiovascular disease [9,10], and, thereby, reducing the likelihood of thrombosis - an important factor in limiting life expectancy [11].

The goal of the study is to determine the ability of aged rats to contain increased platelet aggregation with age by physical exertion.

MATERIALS AND METHODS

The research was conducted in strict accordance with ethical principles established by the European Convent on protection of the vertebrate 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 Russian State Social University (Record №16, dated December, 7th, 2015).

The study included 26 healthy male rats 12 months. Age, which during the year spent daily physical activities on the horizontal treadmill TORNEO of KETLER, moving at a speed of 5m / min. The animals were placed in one of the sections of a wooden frame of a rectangular shape mounted on a treadmill, divided by wooden partitions into 3 parts for the individual placement of the animal. On the first day, the duration of the load was 1 minute, followed by its lengthening by 1 minute per day, bringing it up to 25 minutes per day and following its unchanged duration for a day until the end of the observation [12]. The control group consisted of 91 healthy male colors, including 30 animals of 12 months of age, 32 rats of 18 months and 29 animals of 24 months of age. All animals were healthy throughout the time prior to taking under supervision, and had not previously participated in any experiments.

The intensity of the processes of lipid peroxidation (LPO) of plasma was evaluated by the content of Thiobarbituric acid (TBA)-active products by the Agath-Med complex and acyl hydro peroxides (AGP), taking into account the antioxidant activity of plasma (AOA) [13]. Aggregation of platelets (AP) was elucidated by a visual micro method using ADP (0.5×10^{-4} M), collagen (1: 2 dilution of the main suspension), thrombin (0.125 units / ml), ristomycin (0.8 mg / ml), epinephrine (5×10^{-6} M) and hydrogen peroxide ($7,3 \times 10^{-3}$ M), as well as combinations of ADP and epinephrine; ADP and collagen; epinephrine and collagen. Evaluation of the indicators taken into account in the experimental group was conducted at the time of taking into the study (at the age of 12 months), at 18 months and at 24 months. Three age groups of rats (12 months, 18 months and 24 months) who made the control were examined once. The statistical processing of the results is carried out by Student's t-test.

RESULTS AND DISCUSSION

The observed experimental and control rats of 12 months of age had no differences in all the indicators considered before the start of the study. As the age increased, a significant increase in the amount of AGP and TBA products in plasma was noted in the control with a decrease in its AOA. At the same time, the stability of LPO plasma and its antioxidant protection was characteristic for experimental rats. Thus, at the age of 24 months, the AHP were 1.59 ± 0.019 D₂₃₃/1 ml, the TBA-active products were 3.66 ± 0.021 μmol/l and the AOA value was $32.2 \pm 0.37\%$. In the control 24 monthly rats, these indices were 1.95 ± 0.033 D₂₃₃/1ml, 4.22 ± 0.042 μmol / l and $26.2 \pm 0.27\%$, respectively.

The number and aggregation of platelets in the initial state in both groups of rats were similar. The most active AP developed in these animals under the influence of collagen, later AP came with ristomycin,

H₂O₂ and ADP, even later with thrombin. The latest AT in experimental rats and controls at 12 months. Is marked by the action of epinephrine. Combinations of inductors in them contributed to their mutual potentiating and acceleration of AT, ensuring the onset of AP almost twice as fast as with individual inducters (Table).

Table: Biochemical and hematological parameters in rats of the second year of life against the background of regular physical activity

Indicators	Experienced group, M±m, n=26			Control group, M±m, n=91		
	12 months, n=26	18months, n=26	24months, n=26	12,months n=30	18months, n=32	24months, n=29
Acylhydroperoxides of plasma, D ₂₃₃ /l ml	1.53±0.015	1.56±0.014	1.59±0.019	1.52±0.018	1.60±0.024*	1.95±0.033**
Thiobarbituric acid-products of plasma, umol/l	3.59±0.012	3.62±0.016	3.66±0.021	3.61±0.022	3.80±0.016*	4.22±0.042**
Antioxidant activity of plasma, %	32.8±0.33	32.4±0.29	32.2±0.37	32.6±0.24	30.7±0.32*	26.2±0.27**
aggregation of platelets with ADP, s	40.0±0.10	41.1±0.07	41.6±0.09	39.2±0.08	38.4±0.12*	35.0±0.14**
aggregation of platelets with collagen, s	31.8±0.14	31.6±0.08	30.9±0.12	32.0±0.14	31.8±0.09*	29.6±0.12**
aggregation of platelets with thrombin, s	54.3±0.11	54.0±0.15	53.7±0.08	54.5±0.16	51.3±0.14*	48.6±0.09**
aggregation of platelets with ristomycin, s	46.9±0.10	46.7±0.11	46.1±0.14	47.3±0.13	46.1±0.09*	43.0±0.13**
aggregation of platelets with H ₂ O ₂ , s	42.3±0.08	41.9±0.17	41.6±0.12	42.1±0.10	41.1±0.14*	37.6±0.08**
aggregation of platelets with epinephrine, s	98.2±0.14	97.9±0.16	97.2±0.12	98.1±0.22	93.4±0.16*	88.2±0.17**
aggregation of platelets with ADP and epinephrine,	37.1±0.12	36.7±0.10	36.0±0.07	37.3±0.13	35.2±0.08*	32.6±0.09**
aggregation of platelets with ADP and collagen, s	28.3±0.06	28.1±0.08	27.7±0.07	28.5±0.09	27.6±0.12*	25.2±0.16**
aggregation of platelets with epinephrine and collagen, s	32.1±0.05	31.7±0.07	31.1±0.06	32.3±0.11	31.3±0.07*	29.1±0.10**
Platelets-discocytes, %	78.9±0.22	78.2±0.14	77.9±0.19	79.4±0.18	77.2±0.15*	70.4±0.19**
Sum of platelets' active forms, %	21.1±0.18	21.8±0.15	22.1±0.16	20.6±0.14	22.8±0.19*	29.6±0.17**
number of platelets in the aggregates, %	4.9±0.08	4.9±0.07	5.1±0.09	4.8±0.12	4.9±0.05*	5.9±0.09**
Number of little aggregates (in 100 free platelets)	3.6±0.10	3.7±0.09	3.8±0.12	3.5±0.07	3.6±0.09*	5.7±0.10**
Number of medium and large aggregates (in 100 free platelets)	0.14±0.006	0.15±0.005	0.14±0.006	0.13±0.008	0.17±0.004*	0.38±0.003**

Note: there were no significant differences between 12 months of experimental and control rats and age-related dynamics in experimental rats.

Legend: the reliability of age-related dynamics in the control rats relative to 12 months of age:

* - p <0.05; ** - p <0.01.

In control, as the age increased, there was an increase in the activity of AP in response to all agonists and their combinations. At the same time, under the influence of physical activity in animals at 18 and 24 months, the retention of AP at the level corresponding to 12 months of age was noted. At the same time, the most active platelets of animals that experienced physical exertion reacted to collagen and ADP, slightly weaker for H₂O₂ and ristomycin, even less active on thrombin and epinephrine. The duration of AP in rats in response to combinations of inducers against the background of physical exertion was also maintained at the level of 12 months of age (Table).

Regular physical exertion can have an optimizing effect on the body and platelet hemostasis in conditions of pathology [3]. At the same time, their effect on age-related changes in platelet activity has remained virtually unexplored [14, 15, and 16]. To solve this problem, an assessment of the dynamics of platelet activity in rats was carried out during the 2nd year of life - the stage of their ontogenesis, during which the manifestation of signs of aging increases [2]. In the rats of the control group, activation of plasma LPO and activation of platelet aggregation by all tried inductors and their combinations were noted. At the heart of this lay the intensification in them of the intensity of the exchange of arachidonic acid with the increase in the formation of a powerful aggregate-thromboxane [17, 18]. In addition, judging by the acceleration of AP with ristomycin, in the blood of control rats of the second year of life, the number of cofactors of aggregation, the von Will brand factor, increased [19,20]. The acceleration of AP with the two inducers of aggregation detected in them indicated its increase in the absence of regular physical activity in conditions close to intravascular [21, 22].

Regular daily jogging in the rats during the second year of life was maintained at a level close to the baseline (12 months of life), the intensity of LPO processes in the liquid part of the blood, which weakened its stimulating effect on the surface structures of platelets [23,24]. Sufficiently slowed AP in physically loaded rats is largely a consequence of the stably low intensity of LPO and the optimal state of receptor and post receptor mechanisms of platelet function [25, 26]. The retention of the elongated time of onset of AT under the action of ristomycin indicated a stably low level in the blood of the rats receiving physical exertion, the von Will brand factor [27]. The high resistance of platelets to hydrogen peroxide, marked by the duration of AP in the test with H₂O₂, indicated the preservation of the activity of the platelet ant oxidation system in the observed animals, which further inhibited their aggregation ability with age [28,29].

CONCLUSION

In healthy rats over the age of 12 months there is a gradual increase in the aggregation capacity of platelets with individual inducers and their combinations. Regular daily physical activity in rats between 12 and 24 months of life retains the functional activity of platelets at a normal level, inhibiting the age-related enhancement of their aggregation capabilities.

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