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PATHOPHYSIOLOGICAL SIGNIFICANCE OF CREATINEKINASE AND LACTATEDEHYDROGENASE IN THE MECHANISMS OF ADAPTATION OF MUSCLE TISSUE OF DESCENDANTS

G. F. Stepanov

Odesa National Medical University, Odesa, Ukraine

Abstract

Over the past half century, the human population has seen a significant increase in the proportion of individuals exposed to ionizing radiation. One of the urgent problems of radiobiology is the establishment of the natural radiosensitivity of the organism, which provides the possibility of predicting the remote consequences of radiation exposure. The general condition of animals after ionizing radiation and the changes caused by this radiation largely determine the functioning of muscle tissue, which plays an important role in ensuring the vital activity of the body. The leading pathogenetic factor of radiation damage to the body is a violation of the metabolism and structural organization of enzymatic systems, due to which a sequence of biochemical processes and compartmentalization of enzyme systems change, and their solubilization increases. Additionally, it is extremely important to understand the detailed mechanisms of energy supply for the functioning of muscle tissue in the body of intact animals. The purpose of the work is to determine the pathophysiological significance of creatinekinase and lactatedehydrogenase in the mechanisms of adaptation of the body of the

descendants of intact rats to the influence of a stress factor by studying changes in the activity of creatinekinase and lactatedehydrogenase in the blood and muscle system. A characteristic feature of creatine metabolism in 1-month-old pup rats was shown to be the low content of creatine and creatinine in skeletal and cardiac muscles against the background of low activity of the creatine phosphokinase enzyme in these muscles and its sharp increase in blood. Expressed hypercreatinuria and hypocreatininuria are registered in the blood of 1-month-old pup rats, which can be realized due to the strengthening of biosynthetic processes against the background of the inability of muscle tissue to fix these metabolites. In the skeletal and cardiac muscles of intact 1-month-old pup rats, the activity of creatine phosphokinase is decreased due to the decrease in the activity of the MM -isoform of the enzyme. The investigated metabolic processes in the muscle system of intact animals were shown to be extremely sensitive to the altering influence of ionizing radiation. The authors stressed that understanding the pathophysiological mechanisms of adaptation of the muscular system to the probable influence of a stressful radiation factor, we can draw a conclusion about the depth and severity of the pathological process based on the state of the enzyme systems, and we consider the determination of enzymatic tests in the blood to be important in diagnostic and prognostic aspects.

Key words: irradiated animals; muscle tissue; creatinekinase; lactatedehydrogenase; adaptation; pathophysiological mechanisms

Over the past half century, the human population has seen a significant increase in the proportion of individuals exposed to ionizing radiation [1, 2]. This is caused by environmental pollution due to radiation accidents, an increase in the number of nuclear energy facilities and the military complex, as well as the use of ionizing radiation sources in medical practice and in various technologies [16, 20]. At the same time, it should be noted that there is a significant increase in the number of married couples whose parents were exposed to radiation [2, 17, 21].

One of the urgent problems of radiobiology is the establishment of the natural radiosensitivity of the organism, which provides the possibility of predicting the remote consequences of radiation exposure. Of particular importance are those metabolic processes that undergo the greatest changes under the conditions of ionizing radiation action. The general condition of animals after ionizing radiation and the changes caused by this radiation largely determine the functioning of muscle tissue, which plays an important role in ensuring the vital activity of the body [14, 15, 18, 21, 22]. And if we take into account that the

descendants of irradiated animals, which are exposed to radiation themselves, are subjected to physical stress, then deeper biochemical changes in the metabolism of muscle tissue should be expected [5, 18]. It is known that slight violations of muscle function lead to a significant disintegration of metabolism and a decrease in the body's adaptive capacity [2, 3].

The leading pathogenetic factor of radiation damage to the body is a violation of the metabolism and structural organization of enzymatic systems, due to which a sequence of biochemical processes and compartmentalization of enzyme systems change, and their solubilization increases [5, 8-10, 12].

The biosynthesis of ATP, which is carried out by a system of oxidoreductive enzymes localized in the inner membrane of the mitochondria - the respiratory chain, belongs to the vital processes directly disturbed under the action of ionizing radiation. The high degree of damage to this system is due to the significant radiosensitivity of metal-containing enzymes (which mainly make up the respiratory chain). Violation of bioenergetic processes due to damage to the respiratory chain leads to a deficiency of ATP in the cell, the result of which can be either the death of the cell due to a lack of energy for the functioning of repair systems and the performance of vital functions, or a transition of the cell to a more primitive type of energy supply [13].

With all of the above, it is extremely important to understand the detailed mechanisms of energy supply for the functioning of muscle tissue in the body of intact animals, because in this case, preventive and curative/rehabilitative medical measures should be easier in the case of muscle dysfunction caused by ionizing radiation. We consider it expedient for a better methodological construction of our work to determine the beginnings with the peculiarities of the biochemical supply of energy resources of robotic muscles in an intact organism.

The aim of the work is to determine the pathophysiological significance of creatinekinase and lactatedehydrogenase in the mechanisms of adaptation of the body of the descendants of intact rats to the influence of a stress factor by studying changes in the activity of creatinekinase and lactatedehydrogenase in the blood and muscle system.

Material and Methods

The studies were conducted on sexually mature male rats weighing 180-220 g of the Wistar line, which were kept on a standard vivarium diet. Keeping, processing of the animals and manipulations with them were carried out in accordance with the "General Ethical Principles of Animal Experiments" adopted by the Fifth National Congress on Bioethics (Kyiv, 2013), being guided by the recommendations of the European Convention on the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg,

1985), the methodological recommendations of the State Expert Center of the Ministry of Health Ukraine "Preclinical studies of drugs" (2001) and the rules of humane treatment of experimental animals and conditions approved by the Bioethics Commission of the Odesa National Medical University (protocol No. 32D dated 03/17/2016).

The studies were conducted on 1-month-old pup rats born to intact animals.

The animals were divided into groups as follows:

1. Intact sexually mature animals.

2. 1-month-old pup rats obtained from intact animals. There were 8-10 animals in each group.

Animals were removed from the experiment by euthanasia under propofol (IV, 60 mg/kg) anesthesia. After the animals were dissected, their blood was collected, the heart and the anterior group of thigh muscles were removed. Blood was centrifuged at 3000 g for 10 minutes to obtain serum. The removed cardiac and skeletal muscles were washed with chilled with 0.9% physiological NaCl solution, minced and homogenized in a 9-fold volume of 0.32 mol sucrose per 0.05 mol Tris buffer, pH 7.36 in a homogenizer with Teflon surfaces and subjected to differential centrifugation in a refrigerated centrifuge PC-6. Nuclei were precipitated at 1000g for 10 min., then mitochondria at 12000g for 20 min. were resuspended in a homogenizer in isolation medium containing 0.1% triton X-100 solution at the rate of 1 ml of 0.1% triton solution per 500 mg of tissue and left in ice for 30-35 min.

Mitochondria, mitochondrial supernatant of myocardium, anterior group of thigh muscles and blood serum were used for biochemical studies. Our attention was focused on the activity of lactatedehydrogenase (LDH), creatinekinase (CK) and the content of lactate and pyruvate. To detect the content of biosubstrates in tissues, they were immersed in liquefied nitrogen followed by treatment with perchloric acid [4].

The principle of the method for LDH activity determining consists in the reduction of pyruvate to lactate in the presence of reduced NAD [7]. LDH activity was expressed in μmoles of used $NADH+H^+$ per mg of protein in the sample for 1 min of incubation.

LDH isoenzymes in tissues and blood were detected using electrophoresis in a polyacrylamide gel at a temperature of $+3^0$C.· Electrophoregrams were stained with a substrate mixture (NAD, tetrazolium nitroblue, sodium lactate, phenazine metasulfate, phosphate buffer). After fixing the electrophoregrams, they were dried in a thermostat for 2 hours at a temperature of $+50\ ^0$ C and densitometered. The content of isoenzymes was determined planimetrically [7].

The principle of the method for detecting the content of lactate and pyruvate consists in an enzymatic reaction catalyzed by LDH in the presence of the oxidized or reduced form of NAD, the accumulation or loss of which is recorded spectrophotometrically at 340 nm against the control, where there is no tissue extract, and expressed in μmol per 1 g of tissue [7]. The protein content in the samples was detected by the biuret method [7].

The CK activity in muscles was determined by the initial rate of the reversible reaction of ADP + KrF ↔ATP + creatine at 37 ^{0} C and the incubation time of 3 min. and expressed in nmol of creatine, which was formed, on 1 gram of protein in 1 second, in blood - in nmol/ml per second.

The activity of CK isoenzymes - cardiac (myocardial) isoenzyme (CK-MB), muscle isoenzyme (CK-MB) and mitochondrial isoenzyme (mt-CK) - was determined similarly to the determination of the total catalytic activity of CK, but in the presence of antibodies to certain CK isozyme subunits [4].

Determination of total nitrogen in urine was carried out according to the Kjeldahl method by heating nitrogen-containing organic substances with concentrated sulfuric acid. The principle of the method consists in the mineralization of nitrogen-containing organic substances and the subsequent determination of ammonia by the titrometric method [4].

The obtained data were subjected to statistical processing by the method of estimating the average with the help of "T-tables" using the $\chi 2$ criterion and computer programs. The minimum statistical probability was determined at $p<0.05$.

Results

The creatine-forming system of 1-month-old pup rats born to intact animals is characterized by certain differences from the performance indicators of the creatine-forming system of sexually mature animals.

The content of creatine in the liver of pup rats is significantly lower than that of sexually mature animals. The concentration of creatine in the skeletal and cardiac muscles of intact pup rats is 50.5% and 44.1%, respectively, lower which is significant in comparison with sexually mature animals ($p<0.05$; Table 1).

Creatinine content in cardiac and skeletal muscles is also significantly less than in mature animals. This applies to the enzyme creatinephosphokinase, the activity of which in heart muscle is significantly lower compared to adults, as opposed to skeletal muscle, where its activity does not differ significantly compared to adult animals.

Table 1

The content of components of the creatinekinase system in the tissues of animals of different ages

Researched tissues	Sexually mature animals			1-month-old pup rats		
	Creatine	Creati-nine	Creatine-kinase	Creatine	Creati-nine	Creatine-kinase
Liver, n =8	0.521 ± 0.042	-	-	0.487± 0.038	-	-
Skeletal muscle, n = 8	15.26± 0.96	0.253± 0.054	80.83± 14.7	7.562± 0.48*	0.112± 0.027*	61.26± 11.3
Cardiac muscle, n = 8	9.231± 0.62	0.162± 0.038	6.321± 0.42	5.164± 0.38*	0.086± 0.019	4.283± 0.33*
Blood, n =8	45.21± 8.42	98.43± 15.7	0.724± 0.085	48.16± 8.93	37.62± 7.26*	1.514± 0.161*
Urine, n =8	6.232± 0.52	180.4± 27.3	-	15.32± 1.16*	62.53± 9.35	-

Note: * - $p<0.05$ - probable differences of the studied indicators compared to the corresponding indicators in sexually mature rats

The blood creatine content of 1-month-old pup rats born to intact animals is slightly higher compared to adults, in contrast to creatinine, which is 2.6 times lower compared to intact rats, which is reliable. The CK activity in the blood of 1-month-old pup rats is significantly lower (more than 2 times) compared to adult animals.

As for the excretion of creatine and creatinine with urine, it has a varying character. Compared to adult animals, 1-month-old rats secrete almost 2.5 times more creatine, which is significant ($p<0.05$) , and, on the contrary, 2.9 times less creatinine ($p<0.05$; Table 1).

CK activity in the heart muscle of sexually mature rats is 12.8 times lower than its activity in skeletal muscle ($p<0.05$; Table 2).

CK isozymes in the tissues of sexually mature animals are distributed as follows. In skeletal muscle, the content of the CK-MM-form is 90% of all creatinephosphokinase activity and is 30 times more than the CK-MB-form and 18 times more than the mt-KK-form ($p<0.05$).

In cardiac muscle, the content of the CK-MM-form is 40% of the total activity and it is 2 times higher than the activity of the CK-MB-form ($p <0.05$). The activity of the mitochondrial creatinephosphokinase mt-CK isoenzyme in this muscle is 35% of the total activity.

Table 2

Activity of creatinekinase and its isozymes in tissues of intact sexually mature animals and their 1-month-old descendants

Investigated tissues	Creatinekinase activity (M±m)			
	General	CK-MM	CK-MB	Mt-CK
Intact mature rats				
Skeletal muscle , n =8	80.83±8.00	72.75±7.15	2.425±0.240	4.042±0.390
Cardiac muscle , n =8	6.321±0.420	2.528±0.250	1.264±0.120	2.212±0.210
Blood , n =8	0.724±0.065	0.688±0.060	0.036±0.004	-
1-month - old pup rats born to intact animals				
Skeletal muscle , n =8	61.26±5.50*	56.26±5.42	3.160±0.270*	1.838±0.180*
Cardiac muscle , n =8	4.283±0.330*	1.842±0.180*	1.071±0.090	1.285±0.110*
Blood , n =8	1.514±0.131*	1.430±0.130*	0.076±0.007*	-

Note: * - $p<0.05$ - probable differences of the studied indicators compared to the corresponding indicators in sexually mature rats

Significant differences in the functioning of the CK system are observed in 1-month-old rats (Table 2). This concerns the enzyme creatinephosphokinase, the activity of which in skeletal and cardiac muscle is significantly lower compared to adults.

Characterizing the isozyme spectrum of creatinephosphokinase in 1-month-old rats born from intact animals, it should be noted that the activity of the CK-MM-form in cardiac muscle is 1.37 times less than the activity in adult animals, in skeletal muscle the activity of this isozyme is significantly lower than its activity in adults ($p<0.05$).

The activity of the CK-MB-form of the enzyme in heart muscle is slightly lower compared to sexually mature animals, and its activity in skeletal muscle is 1.3 times higher than in adult animals ($p<0.05$). The activity of mt-CK-form of creatinephosphokinase in cardiac and skeletal muscles is significantly lower compared to sexually mature animals ($p<0.05$).

Skeletal muscle is characterized by high activity of glycolytic processes, and this is reflected in the activity of LDH, which catalyzes the terminal stage of glycolysis (Table 3).

In skeletal muscles of sexually mature animals, LDH activity is almost 1.3 times higher than in heart muscle. In 1-month-old pup rats, LDH activity in both myocardium and skeletal muscle significantly exceeds that of sexually mature animals ($p<0.05$), and 1.4 times higher activity of the enzyme in skeletal muscle compared to myocardium is also observed.

Table 3

Lactatedehydrogenase activity and the content of metabolites in the tissues of intact sexually mature animals and 1-month-old pup rats

The investigated indicators	LDH activity and metabolite content (M ± m)			
	Sexually mature animals		1-month-old pup rats	
	Myocardium	Skeletal muscle	Myocardium	Skeletal muscle
LDH, n=10	1.542±0.076	2.060±0.094	1.876±0.081 *	2.651±0.096 *
Lactate, n=10	2.768±0.191	3.327±0.165	3.286±0.163 *	3.884±0.205 *
Pyruvate, n=10	0.310±0.015	0.332±0.018	0.376±0.017 *	0.406±0.022 *

Note: * - $p<0.05$ - probable differences of the studied indicators compared to the corresponding indicators in sexually mature rats

It leaves its mark on the content of pyruvate and lactate in the tissues. The concentration of these substrates in the myocardium of animals of both age groups is lower than in skeletal muscle. Pyruvate content in the muscles of intact mature animals is only slightly higher than in myocardium, but the amount of lactate is probably higher in skeletal muscle than in the heart, resulting in a cardiac lactate/pyruvate ratio of 8.929, while in the skeletal it reaches 10.021. If we evaluate the absolute indicators, then for both substrates they are significantly higher in 1-month-old pup rats compared to sexually mature animals, but the predominant accumulation of pyruvate reduces the redox potential of lactate/pyruvate in the tissues of 1-month-old pup rats.

The LDH isoenzyme spectrum of the myocardium of sexually mature animals is characterized by a high content of LDH_1 and LDH_2 isoenzymes rapidly migrating to the anode (Table 4).

Table 4

Isoenzyme spectrum of lactatedehydrogenase of myocardium and skeletal muscle of intact sexually mature animals and 1-month-old pup rats

The investigated indicators	Activity of LDH isozymes, % (M ± m)			
	Sexually mature animals		1-month-old pup rats	
	Myocardium	Skeletal muscle	Myocardium	Skeletal muscle
LDH_1, n=10	35.2±0.8	0.9±0.04	30.4±0.7 *	0.4±0.04 *
LDH_2, n=10	34.7±0.9	2.8±0.3	29.3±0.8 *	1.2±0.1 *
LDH_3, n=10	24.5±0.6	10.1±0.7	26.5±0.5	6.6±0.4 *
LDH_4, n=10	4.9±0.5	13.2±1.1	9.4±1.0 *	15.8±1.2
LDH_5, n=10	0.7±0.1	73.1±1.9	4.4±0.5 *	76.0±4.0

Note: * - $p<0.05$ - probable differences of the studied indicators compared to the corresponding indicators in sexually mature rats

They account for 70% of LDH enzymatic activity in this tissue. Much less is contained in the tissue of the third fraction of the enzyme, and the amount of LDH_4 and, especially, LDH_5 is extremely small. If LDH_3 provides almost 25% of enzymatic activity in the heart, then LDH_4 is about 5% and LDH_5 is up to 1%.

The LDH isoenzyme spectrum of skeletal muscles of sexually mature animals is mainly represented by the fifth isoenzyme, which reaches almost ¾ of the total activity of the enzyme in this tissue. Its activity is more than 5 times higher than LDH_4 and 7 times higher than LDH_3 . The content of LDH_2 and LDH_1 is approximately 3% and 1%, respectively, of the total activity of the enzyme.

If we take into account that fast-migrating LDH isoenzymes are inhibited by small concentrations of pyruvate and its optimal concentration for LDH_1 is almost 10 times lower than for LDH_5 , as well as the fact that the pyruvate kinase reaction, the product of which is pyruvate, in skeletal muscles is several times higher than that of the heart, the predominant accumulation of lactate in the skeletal muscles becomes clear. So, if most of the pyruvate formed in skeletal muscles is used for lactate synthesis, then in the myocardium, pyruvate, undergoing oxidative decarboxylation, enters oxidation reactions in the cycle of tricarboxylic acids.

A feature of the LDH isozyme spectrum in the tissues of rat pup rats is that the content of LDH_1 and LDH_2 is significantly reduced in the myocardium . Their amount is 1.2 and 1.13 times smaller, respectively, compared to sexually mature animals. In this context, the content of LDH_3 slightly increases , the content of LDH_4 is twice as high, and the content of LDH_5 is more than 6 times higher than the indicators of sexually mature animals. In skeletal muscles of pup rats, the dominant content of LDH_5 and LDH_4 increases and this occurs due to a decrease in the activity of LDH_3 (more than 1.5 times), LDH_2 (more than 2.3 times) and LDH_1 (2 .2 times) compared to sexually mature animals. The obtained data indicate that in the myocardium and skeletal muscles of pup rats a higher percentage of isoenzymes formed from M-subunits, which function in anaerobic conditions, and with age the content of H-subunits increases as a result of epigenetic changes. This is confirmed by the general activity of the enzyme and the content of pyruvate and lactate metabolites in both tissues.

Discussion

Thus, our data highlighted certain interesting points of biochemical maintenance of muscle contraction of different types of muscles in rats of different ages. The interest in the obtained data, which is a fragment of the scientific research devoted to the study of the pathophysiological mechanisms of adaptation of muscle tissue under the action of ionizing

radiation, lies in the fact that immediately before elucidating the biochemical energy processes characteristic of muscles, it is important to determine the features of their manifestation according to normal conditions. At the same time, of course, bearing in mind the peculiarities of perspective muscle work in response to stressful effects of any genesis and etiology is also very important.

To determine the energy supply of muscle tissue, it was important to find out the direction of metabolism towards aerobic or anaerobic processes. In this regard, the reaction of glycolytic substrate phosphorylation catalyzed by pyruvate kinase which provides half of the energy released from glucose in the glycolytic process and the LDH reaction coupled with it, as well as the reactions of the Krebs cycle, in particular the NAD-dependent malate dehydrogenase reaction, which competes in the cytoplasm of cells for nicotinamide coenzymes with LDH and performs a shuttle function in the transport of reduced equivalents through the mitochondrial membrane are of significant importance [5].

Carbohydrate resynthesis plays a major role in maintaining the functional activity of tissues. However, due to the fact that the pyruvate kinase reaction is irreversible, the resynthesis of phosphoenolpyruvate from pyruvate, oxaloacetate and other products of a non-carbohydrate nature is carried out through a number of intermediate stages that are catalyzed due to the absence of pyruvate carboxylase, phosphoenolpyruvate carboxykinase and decarboxylating NADP-dependent malate dehydrogenase in muscle tissue. A characteristic feature of these enzymatic systems is that they either use compounds including B vitamins as coenzymes, or their functional activity depends on the number of these coenzymes and the coenzyme redox system [19].

Another positive, in our opinion, aspect of the performed work and the obtained data is the age dependence of the activity of the studied CK and LDH systems in the body of sexually mature and 1-month-old animals. This methodological construction of the work will give us the opportunity to compare these data under normal conditions with analogous results, which will highlight the nature of muscle supply in rats of different ages due to the influence of ionizing radiation. Moreover, from a prospective point of view, it is important that the peculiarities of muscle metabolism in the descendants of intact sexually mature rats are being investigated, which will later logically coincide with the obtained data, which should characterize the pathophysiological mechanisms of the reconstruction of the work of the muscle system in the descendants of irradiated rats.

The biosynthesis of ATP, which is carried out by the system of oxidoreductive enzymes localized in the inner membrane of the mitochondria of the respiratory chain, belongs to the

vital processes that are directly disrupted under the action of ionizing radiation. The high degree of damage to this system is due to the significant radiosensitivity of metal-containing enzymes (which mainly make up the respiratory chain) [5, 6, 9]. Violation of bioenergetic processes due to damage to the respiratory chain leads to a deficiency of ATP in the cell, the result of which can be either the death of the cell due to a lack of energy for the functioning of repair systems and the performance of vital functions, or a transition of the cell to a more primitive type of energy supply [9, 11, 15].

Therefore, a characteristic feature of creatine metabolism in 1-month-old pup rats is a rather low content of creatine and, as a result, creatinine in skeletal and cardiac muscles compared to intact animals against the background of low activity of the creatinephosphokinase enzyme in these muscles and a sharp increase in it in the blood. The pronounced hypercreatinuria and hypocreatininuria demonstrated by us is apparently related to the strengthening of biosynthetic processes in 1-month-old pup rats against the background of the inability of muscle tissue to fix these metabolites.

The analysis of the obtained data indicates a decrease in the activity of creatinephosphokinase in the skeletal and cardiac muscles of intact 1-month-old pup rats when compared with this indicator in sexually mature animals. These consequences occur mainly due to a decrease in the activity of the MM isoform of the enzyme, while the MB isoform of the enzyme in the myocardium is not significantly changed, and in the skeletal muscle it exceeds the indicators of sexually mature animals by a third. The activity of the mitochondrial form of the enzyme is almost twice as low as in adult animals.

Summarizing the above, it should be concluded that, unlike skeletal muscle, the activity of the tricarboxylic acid cycle, in particular the NAD-dependent malate dehydrogenase, in the myocardium is quite significant both in the cytoplasm and in the mitochondria of the tissue, as evidenced by the higher level of tricarboxylic acid cycle metabolites acids - malic and oxaloacetic, as well as the activity of NADP-dependent malate dehydrogenase, which plays a connecting role between glycolysis and the cycle of tricarboxylic acids in providing them with metabolites and transferring protons from NADH + H^+ to NADP [5, 9]. As a result, the myocardium is characterized by a larger pool of adenyl nucleotides due to ATP.

In the myocardium and skeletal muscles of pup rats, the percentage of LDH isoenzymes formed from M-subunits is higher, and with age, as a result of epigenetic changes, the content of H-subunits increases, which affects the direction of carbohydrate metabolism in the tissues of sexually mature animals.

We emphasize the fact that the metabolic processes we investigated in the muscular system of intact animals are extremely sensitive to the altering influence of ionizing radiation. And because of this, by understanding in detail the pathophysiological mechanisms of adaptation of the muscular system to the influence of a stress factor, it is possible to draw a conclusion about the depth and severity of the pathological process based on the state of the enzyme systems, and we consider the determination of enzymatic tests in the blood to be important in diagnostic and prognostic aspects.

Conclusions

The obtained data have highlighted interesting points of biochemical maintenance of muscle contraction of different types of muscles in rats of different ages. A characteristic feature of creatine metabolism in 1-month-old pup rats is the low content of creatine and creatinine in skeletal and cardiac muscles against the background of low activity of the creatinephosphokinase enzyme in these muscles and its sharp increase in blood.

Expressed hypercreatinuria and hypocreatininuria are registered in the blood of 1-month-old pup rats, which can be realized due to the strengthening of biosynthetic processes against the background of the inability of muscle tissue to fix these metabolites.

In the skeletal and cardiac muscles of intact 1-month-old pup rats, the activity of creatinephosphokinase is decreased due to the decrease in the activity of the MM -isoform of the enzyme.

The investigated metabolic processes in the muscular system of intact animals are extremely sensitive to the altering influence of ionizing radiation. Understanding the pathophysiological mechanisms of adaptation of the muscular system to the probable influence of a stressful radiation factor, we can draw a conclusion about the depth and severity of the pathological process based on the state of the enzyme systems, and we consider the determination of enzymatic tests in the blood to be important in diagnostic and prognostic aspects.

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Stepanov G.F. - conceptualization, methodology, formal analysis, data curation, writing—original draft preparation, writing—review and editing, supervision.

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The experimental studies were carried out in the conditions of a chronic experiment in accordance with international standards of humane treatment of vertebrate animals and

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Informed Consent Statement

The data of experimental studies are given. Written informed consent from the patients was not necessary to publish this paper.

Data Availability Statement

The data presented in this study are available on request from the corresponding author.

Conflicts of Interest

The author declare no conflict of interest.