Stepanov H. F., Dubna Ye. S., Vastyanov R. S., Mokriienko E. M., Buriachkivskyi E. S. Mechanisms of muscle tissue adaptation in response to the influence of low-dose ionizing radiation. Journal of Education, Health and Sport. 2024;68:55493. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2024.68.55493
https://apcz.umk.pl/JEHS/article/view/55493
https://zenodo.org/records/13882753

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences);
Health Sciences (Field of medical and health sciences). Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
Received: 21.08.2024. Revised: 17.09.2024. Accepted: 21.09.2024. Published: 24.09.2024.

UDC: 614.876:616-055.6:577.122:616-092.4

MECHANISMS OF MUSCLE TISSUE ADAPTATION IN RESPONSE TO THE INFLUENCE OF LOW-DOSE IONIZING RADIATION

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Abstract

Mechanisms of interaction of ionizing radiation with biological objects are a chain of successive physical and physico-chemical changes, which manifest themselves in the form of excitation, primary and secondary ionization of molecules. Biosynthesis of ATP, which is carried out by a system of oxidation-reduction enzymes localized in the inner membrane of mitochondria - the respiratory chain, belongs to the vital processes that are 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. The purpose of the work is to study the formation of the adaptive response of muscle tissue of sexually mature rats to the influence of ionizing radiation at a dose of 0.5 Gy. It was concluded that a day after irradiation with the dose of 0.5 Gy, the content of contractile proteins in skeletal muscle decreases slightly. On the 15th day, the content of contractile proteins began to decrease. By the 30th day, the content of contractile proteins decreased by 22.9% for myosin, by more than 11% for actin, and by 7 and 8% for troponin and tropomyosin, respectively, compared to the values of the intact group. A similar picture is observed in the cardiac muscle. Mg^{2+},Ca^{2+}-ATP-ase activity of actomyosin, starting from the 1st day was shown to be increased in both the skeletal and cardiac muscles, reaching its peak in the cardiac muscle on the 15th day, in contrast to the skeletal muscle, where this indicator reached its peak on the 7th day. The authors conclude that irradiation of sexually mature animals with the dose of 0.5 Gy forms an adaptive response that is accompanied by an increase in Mg^{2+},Ca^{2+}-ATP-ase activity due to the formation of a strong form of binding between F-actin and myosin, actin monomers go into the typical for actomyosin "turned on stage", and the myosin heads acquire an ordered orientation in the muscle fiber. According to author's idea, the data obtained indicated the benefit and reasonability of using in post-radiation dysfunctions complex pharmacological treatment drugs that are able to normalize intracellular homeostasis, eliminate probable acidic changes initiated by radiation exposure, activate the processes of intramuscle energy generation and which have protective properties in relation to the muscular system.

Key words: muscle tissue; skeletal muscle; cardiac muscle; ionizing irradiation; energy; adaptation; pathophysiological mechanisms

Mechanisms of interaction of ionizing radiation with biological objects are a chain of successive physical and physico-chemical changes, which manifest themselves in the form of excitation, primary and secondary ionization of molecules, which, in turn, leads to the appearance of excited atoms and free radicals that react with one another and with intact biomolecules. The development of free radical processes leads to membrane damage and covalent binding of metabolites, which in turn leads to a violation of oxidative phosphorylation and cell energy [8]. Most authors explain the remote effects of the adverse influence of exogenous factors with the given mechanism. Their development depends on the accumulation of reactive metabolites, the hormonal function of the hypothalamus, which is a "conductor" of the body's adaptive responses to environmental factors [11-13].

Biosynthesis of ATP, which is carried out by a system of oxidation-reduction enzymes localized in the inner membrane of mitochondria - the respiratory chain, belongs to the vital processes that are 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 an acute shortage of ATP in the cell, the result of which can be either death of the cell due to a lack of energy for the functioning of repair systems and the performance of vital functions, or the transition of the cell to a more primitive type of energy supply [1, 18].

In experiments aimed at studying the adaptive response, in addition to a decrease in body weight, an increase in the relative weight of the spleen and liver was found in chronically irradiated animals, which probably indicates an increase in the load on these organs during the irradiation process, the cause of which may be a more active destruction of blood cells than in animals developing without exposure to radiation [7, 15].

One of general manifestations of adaptation is a change in motor activity [2, 16], which manifests itself, in particular, in a change in muscle function, muscle contraction, but the biochemical mechanisms of adaptation of muscle tissue in response to the impact of ionizing radiation are not finally defined.

The aim of the work is to study the formation of the adaptive response of muscle tissue of sexually mature rats to the influence of ionizing radiation at a dose of 0.5 Gy.

Material and methods

The studies were conducted on sexually mature male rats weighing 180- 220 g. of Wistar line 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), 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 Odesa National Medical University (record No. 32D dated 17.03.2016).

The animals were subjected to total gamma irradiation of Co^{60} on an empty stomach using the "Agat" telegammatherapy unit. The absorbed dose was 6.0 Gy, the dose rate was 0.48 Gy/min, and the distance to the absorption source was 75 cm. The lethality with this method of irradiation was equal to 43.0% of irradiated animals in 1 month.

The animals were divided into groups as follows: 1. Intact sexually mature animals. 2. Mature animals irradiated at a dose of 0.5 Gy. There were 7-10 animals in each group.

The animals were removed from the experiment by euthanasia under propofol (IV, 60 mg/kg) anesthesia. After the animals were dissected, blood was collected, the heart and the anterior group of thigh muscles were removed. The removed cardiac and skeletal muscles were washed with chilled 0.9% physiological NaCl solution, minced and homogenized in a 9-fold volume of 0.32 mol sucrose at 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., 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.

The ATPase activity of actomyosin and myosin was determined by the amount of inorganic phosphate (P*i*) formed as a result of ATP hydrolysis, according to the Fiske-Subbarow method [5].

Since MDH catalyzes the interconversion of malate into oxaloacetate, the activity was studied both in the direction of malate-oxaloacetate (direct reaction) and oxaloacetate-malate (reverse reaction). The principle of determining the activity of the direct reaction [5] consists in the oxidation of malate to oxaloacetate in the presence of NAD, the activity of the enzyme was assessed by the rate of NAD reduction, which is recorded spectrophotometrically by the increase in optical density at 340 nm.

The activity of MDH was determined in the mitochondrial supernatant, mitochondria of the myocardium and skeletal muscles and was expressed in the myocardium and cytoplasm of the skeletal muscle in μmol of formed NADH per mg of protein in the sample in 1 min of incubation, in the mitochondria of skeletal muscle - in nmol of formed NADH per mg of protein in 1 min of incubation.

The principle of determining the activity of the reverse reaction [14] consists in the reduction of oxaloacetate to malate in the presence of NADH, the activity of the enzyme was expressed in μmol of the lost NADH per mg of protein in the sample in 1 min of incubation.

NADP-dependent MDH catalyzes the interconversion of malate into pyruvate, so the activity of the enzyme was studied both in the direction of malate-pyruvate (direct reaction) and pyruvate-malate (reverse reaction).

The principle of detecting the activity of the direct reaction [3] consists in the oxidative decarboxylation of malate into pyruvate in the presence of NADP. The activity of the enzyme was assessed by the rate of reduction of NADP spectrophotometrically by the increase in optical density at 340 nm and expressed in nmol of formed NADPH per mg of protein in 1 min of incubation.

The principle of detecting the activity of the reverse reaction consists in the carboxylation of pyruvate into malate in the presence of NADPH and HCO_3-. The activity of the enzyme was assessed by the rate of oxidation of NADP, which was recorded spectrophotometrically by the loss of optical density at 340 nm and expressed in nmol of oxidized NADP per mg of protein in the sample in 1 min of incubation.

The content of malate and oxaloacetate was determined according to the method [5] and expressed in μmol per 1 g of tissue (for malate) and in nmol per 1 g of tissue (for oxaloacetate).

The content of adenosine triphosphate (ATP) was determined according to the method [9]. The content of adenosine diphosphate (ADP) and adenosine monophosphate (AMP) in tissues was determined in one sample using combined reactions [9]. All indicators of energy metabolism were expressed in μmol per 1 g of the studied tissue.

Simulation of physical load was carried out by swimming of the animals in water at the temperature of 25–26 °C in a bowl with an extra weight, which was 10% of the weight of the experimental animals.

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

As a result of the research, it was established that a day after irradiation with a dose of 0.5 Gy, the content of contractile proteins in skeletal muscle decreases slightly, but its increase is observed later. On the 15th day, the content of contractile proteins began to decrease, but slightly exceeded this indicator in intact animals. By the 30th day, the content of contractile proteins decreased by 22.9% for myosin, by more than 11% for actin, and by 7 and 8% for troponin and tropomyosin, respectively, compared to the values of the intact group (Table 1).

Table 1

The content of contractile proteins in the skeletal muscle of sexually mature animals irradiated with the dose of 0.5 Gy (μmol per 1 g of tissue)

Investigated indicators	Intact rats, n=10	Irradiated rats within				
		1 day, n=10	3 days, n=10	7days, n=9	15 days, n=9	30 days, n=9
Skeletal muscle						
Myosin	8,92±5,65	8,23±5,64	9,14±5,67	9,29±5,68	9,02±5,63	8,02±5,61
Actin	3,96±0,38	3,25±0,37	4,07±0,42	4,21±0,43	4,02±0,41	3,08±0,34
Troponin	1,69±0,21	1,32±0,21	1,72±0,23	1,96±0,24	1,71±0,22	1,07±0,18
Tropomyosin	1,83±0,16	1,56±0,15	1,89±0,18	1,97±0,19	1,83±0,17	1,16±0,12
Cardiac muscle						
Myosin	9,72±5,85	9,41±5,84	9,88±5,87	9,94±5,88	9,76±5,85	9,92±5,86
Actin	4,53±0,41	4,34±0,39	4,62±0,43	4,73±0,45	4,51±0,41	4,68±0,42
Troponin	1,84±0,18	1,65±0,19	1,91±0,19	1,98±0,21	1,87±0,18	1,93±0,19
Tropomyosin	1,98±0,24	1,78±0,23	2,01±0,26	2,12±0,27	2,01±0,26	2,09±0,25

A similar picture is observed in the cardiac muscle, with the exception of the 30th day, where these indicators in the cardiac muscle, unlike the skeletal muscle, on the contrary, increase compared to the indicators in the cardiac muscle of the intact group.

The results of the conducted studies showed that irradiation with a dose of 0.5 Gy affects both Mg^{2+},Ca^{2+}-ATP-ase and K+-ATP-ase activity, but it changes differently. Mg^{2+},Ca^{2+}-ATP-ase activity of actomyosin, starting from the 1st day, increased in both the skeletal and cardiac muscles, reaching its peak in the cardiac muscle on the 15th day, in contrast to the skeletal muscle, where this indicator reached its peak on the 7th day, and starting from the 15th day, its gradual decrease was observed; in cardiac muscle, a slight decrease was recorded only on the 30th day, but still, this indicator in both the skeletal and cardiac muscles was greater compared to the indicator in intact animals (Tables 2 and 3).

Table 2

ATP-ase activity of actomyosin and myosin in the skeletal muscle of sexually mature animals irradiated with the dose of 0.5 Gy (nmol P*i*/min per mg of protein)

Investigated indicators	Intact rats, n=10	Irradiated rats within				
		1 day, n=10	3 days, n=10	7days, n=9	15 days, n=9	30 days, n=9
Mg^{2+},Ca^{2+}-ATP-ase activity of actomyosin	96,50± 11,32	115,20± 11,89	138,10± 12,34*	142,40± 12,58*	136,30± 12,26*	132,80± 12,18
K^{+}-ATP- ase activity of actomyosin	17,80± 2,76	16,70± 2,73	16,10± 2,72	15,80± 2,69	15,60± 2,68	16,30± 2,71
Mg^{2+},Ca^{2+}-ATP-ase activity of myosin	104,20± 8,52	112,40± 8,56	114,70± 8,58	115,30± 8,57	116,20± 8,59	112,90± 8,54
K^{+}-ATP- ase activity of myosin	50,60± 3,26	50,10± 3,25	50,80± 3,27	51,20± 3,28	50,90± 3,26	50,70± 3,25

Note. *- $p<0.05$ – probable differences of the studied indicators compared to the corresponding indicators in intact animals.

Table 3

ATP-ase activity of actomyosin and myosin in the cardiac muscle of sexually mature animals irradiated with the dose of 0.5 Gy (nmol P*i*/min per mg of protein)

Investigated indicators	Intact rats, n=10	Irradiated rats within				
		1 day, n=10	3 days, n=10	7days, n=9	15 days, n=9	30 days, n=9
Mg^{2+},Ca^{2+}-ATP-ase activity of actomyosin	108,80± 10,66	111,60± 11,21	119,80± 12,16	123,20± 12,28	123,90± 12,27	120,80± 12,26
K^{+}-ATP- ase activity of actomyosin	24,80± 3,16	23,70± 3,15	23,10± 3,14	22,80± 3,12	22,30± 3,11	23,80± 3,15
Mg^{2+},Ca^{2+}-ATP-ase activity of myosin	116,90± 6,84	117,80± 6,85	118,40± 6,87	119,10± 6,86	124,90± 6,89	117,80± 6,85
K^{+}-ATP- ase activity of myosin	52,88± 3,30	52,63± 3,27	52,58± 3,26	52,49± 3,27	52,38± 3,23	52,59± 3,28

As for K^+-ATP-ase activity of actomyosin in cardiac and skeletal muscles, it, starting from the 1st day, decreased compared to this indicator in intact animals. Its gradual increase was observed only on the 30th day, but still it was lower than the indicator in intact animals.

Comparing data on the effect of ionizing radiation at the dose of 0.5 Gy on ATPase activity, it can be assumed that small doses of radiation form a positive adaptive response, which is accompanied by an increase in Mg^{2+},Ca^{2+}-ATP-ase activity due to the formation between F-actin and myosin of a strong form of binding, actin monomers go into the typical for actomyosin "turned on stage", and the myosin heads acquire an ordered orientation in the muscle fiber. An increase in Mg^{2+},Ca^{2+}-ATP-ase activity and a decrease in K+-ATP-ase activity may be associated with the predominance of AM•ADP•P_i and AM•ADP•P*i* intermediates.

In the case of action of ionizing radiation with a dose of 0.5 Gy on pure myosin, data on an increase in Mg^{2+},Ca^{2+}-ATP-ase activity of myosin compared to the control on the 1st, 3rd and 7th days, and a slight decrease in it on 30th day after irradiation in both cardiac and skeletal muscles were obtained.

K^+-ATP-ase activity of myosin practically did not change at all times after irradiation compared to the indicator in intact animals (Tables 2 and 3).

Later, attention was focused on determining the activity of different forms of malate dehydrogenases and the content of their metabolites.

In the cytoplasm of the myocardium of the animals irradiated at the dose of 0.5 Gy, the activity of the direct malate dehydrogenase reaction is slightly reduced, in contrast to the mitochondrial fraction, where its activity is 1.3 times higher than this indicator in intact animals. Opposite changes are observed with the activity of reverse malate dehydrogenase, where its activity in the cytoplasm slightly increases, and in the mitochondria, on the contrary, its significant decrease is observed (Table 4).

In the skeletal muscle of the animals irradiated with the dose of 0.5 Gy, diametrically opposite changes in the activity of the cytoplasmic fraction of the direct and reverse malate dehydrogenase reactions are observed compared to the indicators in the cytosol of the myocardium of this group of animals. This probable increase in the activity of the direct malate dehydrogenase reaction in the cytoplasm and a slight decrease in the reverse malate dehydrogenase reaction is compared to intact animals.

In the mitochondria of skeletal muscle, there is an increase in the activity of the direct malate dehydrogenase reaction, similar to the change in activity in the mitochondria of the myocardium, and a decrease in the activity of the reverse malate dehydrogenase reaction compared to intact animals. In the blood of the studied group of animals, there is a decrease in the activity of both direct and reverse malate dehydrogenase reactions compared to intact animals.

The concentration of malate and oxaloacetate in tissues also changes. If the content of malate in both the cardiac and skeletal muscles decreases, then the changes in the concentration of oxaloacetate compared to intact animals are opposite, namely: against the background of a decrease in the content of this metabolite in the myocardium, its increase is observed in the skeletal muscle, as a result of which the ratio of malate /oxaloacet in the myocardium is 9.079, and in skeletal muscles - 9.045.

Table 4

Activity of NAD- and NADP-dependent malatedehydrogenases and the content of reaction metabolites in the tissues of animals irradiated by 0.5 Gy (n=10)

Investigated substances	Activity of enzymes and metabolites (M±m)				
	Miocardium		Skeletal muscle		Blood
	Cyto-plasm	Mito-chondria	Cyto-plasm	Mito-chondria	
NAD-MDH (direct reaction)	0,482±0,012*	0,178±0,012*	0,294±0,014*	44,102±2,834	1,628±0,154
NAD-MDH (reverse reaction)	2,786±0,132*	0,174±0,008*	1,686±0,088	64,986±2,538	3,462±0,254
Direct/reverse reaction	0,173	1,241	0,174	0,679	0,470
NADP- MDH (direct reaction)	12,928±0,614		7,852±0,578		
NADP- MDH (reverse reaction)	21,978±1,194		11,834±0,526		
Direct/reverse reaction	0,588		0,664		
Malat	0,388±0,022		0,292±0,024		0,124±0,006
Oxaloacet	42,734±1,812		32,284±1,836		14,96±1,08
Malat / oxaloacet	9,079		9,045		8,289

Notes:

1. The activity of NAD-MDH in the myocardium and cytoplasm of skeletal muscle is expressed in μmol/mg of protein for 1 min of incubation;

2. NAD-MDH activity in skeletal muscle mitochondria, blood serum, as well as NADP-MDH activity in tissues is expressed in nmol/mg of protein in 1 min of incubation;

3. Malate content is expressed in μmol/g, oxaloacetate - in nmol/g tissue;

* – $p<0.05$ – probable differences of the studied indicators compared to the corresponding indicators in intact animals.

As mentioned above, NADP-dependent decarboxylating MDH (NADP-MDH) takes an active part in the interconversions of malate and pyruvate, the activity of which in convertion of malate into pyruvate (direct reaction) is slightly reduced in cardiac and increased in skeletal muscles of animals irradiated with the dose of 0, 5 Gy. But the activity of NADP-dependent decarboxylating MDH with regard to the conversion of pyruvate into malate (the reverse reaction) has a diametrically opposite nature of changes. While its increase is observed in the cardiac muscle, in the skeletal muscle, on the contrary, there is a tendency to its decrease, which indicates a greater intensity of oxidative processes in the cardiac muscle.

The ratio of the direct to reverse NADP-dependent decarboxylative malate dehydrogenase reaction increases in skeletal muscle and decreases in cardiac muscle compared to intact animals.

Characterizing the changes in the activity of the direct and reverse NAD, NADP - malate dehydrogenase reaction, as well as the content of malate and oxaloacetate in the tissues of the studied group of animals, it should be noted that the aerobic oxidation process intensifies and the energy resources of muscle tissue increase.

Indicators of energy metabolism in muscle tissue do not differ significantly from intact sexually mature animals (Table 5).

Table 5

The content of ATP, ADP, AMP in the tissues of sexually mature animals irradiated with the dose of 0.5 Gy (n=8)

Investigated tissue	Intact animals			Irradiated with the dose of 0,5 Gy		
	Investigated substances (M±m)					
	ATP µmol/g	ADP µmol/g	AMP µmol/g	ATP µmol/g	ADP µmol/g	AMP µmol/g
Skeletal muscle	3,200± 0,260*	0,425± 0,050*	0,276± 0,030*	3,240± 0,260	0,344± 0,040	0,307± 0,040
Cardiac muscle	5,290± 0,480	0,271± 0,030	0,151± 0,015	5,340± 0,490	0,245± 0,030	0,163± 0,020

A slight increase in the content of ATP and AMP in cardiac and skeletal muscles is observed, and the concentration of ADP in these muscles is insignificantly reduced compared to non-irradiated rats.

As a result, during exercise in animals irradiated with the dose of 0.5 Gy, physical performance increases by almost 10% compared to the intact group (Table 6).

Table 6

Physical performance of intact and irradiated animals (n=9)

Investigated indicator	Indicator of physical performance (M±m)	
	Intact rats	Animals, irradiated with the dose of 0,5 Gy
Swimming time of animals, min	25,74±1,76	28,30±1,82

Discussion

Thus, our data highlighted certain interesting points regarding the formation of the adaptive response of the muscle tissue of sexually mature rats under the conditions of exposure to a low dose of ionizing radiation. The interest in the obtained data, which is a fragment of 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 the contractile function according to conditions of the pathology.

The main functional characteristic of actomyosin is ATPase activity. Since the process of muscle contraction is associated with the formation of the actomyosin complex and its subsequent conformational changes due to the energy released as a result of the enzymatic splitting of ATP by myosin, the ATPase activity of actomyosin is such a characteristic of actomyosin that can be used to judge its capacity for contractile activity of muscles. Mg^{2+},Ca^{2+}-ATPase activity is detected in the presence of Mg^{2+}, Ca^{2+} ions in the environment, which are necessary for muscle contraction.

It was established that the effect of ionizing radiation at tha dose of 0.5 Gy on ATPase activity forms a positive adaptive response, which is accompanied by an increase in Mg^{2+},Ca^{2+}-ATPase activity due to the formation of a strong form of binding between F-actin and myosin, actin monomers go into the typical for actomyosin "turned on stage", and the myosin heads acquire an ordered orientation in the muscle fiber. An increase in Mg^{2+},Ca^{2+}-ATP-ase activity and a decrease in K^{+}-ATP-ase activity may be associated with the predominance of AM•ADP•P*i* and AM•ADP•P*i* intermediates.

The biosynthesis of ATP, which is carried out by a system of oxidation-reduction enzymes localized in the inner membrane of the mitochondria of the respiratory chain, the functioning of which largely depends on the coordinated operation of shuttle mechanisms for the transport of reduced equivalents, is among the vital processes directly disturbed by the action of ionizing radiation. Violation of bioenergetic processes due to damage to the shuttle mechanisms for the transport of reduced equivalents leads to a malfunction of the respiratory chain and, as a result, to a deficiency of ATP in the cell, the result of which can be either the death of the cell due to the lack of energy for the functioning of repair systems and the performance of vital functions, or the transition of the cell to a more primitive type of energy supply.

One of the mechanisms of transport of protons from the sarcoplasm, where they accumulate under load conditions, to the mitochondria, where they are involved in tissue respiration with the release of a significant amount of energy, is the functioning of NAD-dependent malate dehydrogenase, which occupies a special place in muscle bioenergetics [6].

Mitochondrial MDH which catalyzes the oxidation of malate into oxaloacetate, participates in the Krebs cycle and characterizes the final stage of this aerobic oxidation process, while the cytoplasmic form, using oxidized nicotinamide coenzymes, ensures the accumulation of protons in the cytoplasm and leads to the development of acidosis.

In the cytoplasm of the myocardium of animals irradiated at the dose of 0.5 Gy, the activity of the direct MDH reaction is slightly reduced, in contrast to the mitochondrial fraction, where its activity is 1.3 times higher than this indicator in intact animals. Opposite changes are observed with the activity of reverse malate dehydrogenase, where its activity in the cytoplasm slightly increases, and in the mitochondria, on the contrary, its significant decrease is observed.

In the skeletal muscle of animals irradiated with a dose of 0.5 Gy, diametrically opposite changes in the activity of the cytoplasmic fraction of the direct and reverse MDH are observed compared to the indicators in the cytosol of the myocardium of this group of animals. This is a probable increase in the activity of the direct MDH reaction in the cytoplasm and a slight decrease in the reverse MDH reaction compared to intact animals.

In the mitochondria of skeletal muscle, there is an increase in the activity of the direct MDH reaction, similar to the change in activity in the mitochondria of the myocardium, and a decrease in the activity of the reverse MDH reaction compared to intact animals. In the blood of the studied group of animals, there is a decrease in the activity of both direct and reverse MDH reactions compared to intact animals.

Characterizing the changes in the activity of the direct and reverse NAD, NADP - malate dehydrogenase reaction, as well as the content of malate and oxaloacetate in the tissues of the studied group of animals, it should be noted that the aerobic oxidation process intensifies and the energy resources of muscle tissue increase.

As a result, there is a slight increase in the content of ATP and AMP in cardiac and skeletal muscles, and the concentration of ADP in these muscles is insignificantly reduced compared to non-irradiated rats.

The result of the above-mentioned changes in the muscle tissue of animals irradiated with a dose of 0.5 Gy is an increase in their physical capacity by almost 10% compared to the intact group.

The data obtained are a key point in the complex experimental work, one of the tasks of which is the development of a scheme for complex pathogenetically orienetd correction of ionizing radiation induced body's organs and systems disorders. These data analysis indicates the benefit and reasonability of using in post-radiation dysfunctions complex pharmacological treatment drugs that are able to normalize intracellular homeostasis, eliminate probable acidic changes initiated by radiation exposure, activate the processes of intramuscle energy generation and which have protective properties in relation to the muscular system. Multivitamins or a hormone-vitamin complex might be a likely candidates for a similar pharmacotherapeutic effect [4, 17, 19].

Conclusions

1. The obtained data highlighted interesting points regarding the formation of the adaptive response of muscle tissue to the influence of ionizing radiation at the dose of 0.5 Gy.

2. Studying the features of energy metabolism and contractile function of cardiac and skeletal muscles of animals irradiated with the dose of 0.5 Gy, it was established that a day after irradiation with the dose of 0.5 Gy, the content of contractile proteins in skeletal muscle decreases slightly, but its increase is observed later. On the 15th day, the content of contractile proteins began to decrease, but slightly exceeded this indicator in intact animals. By the 30th day, the content of contractile proteins decreased by 22.9% for myosin, by more than 11% for actin, and by 7 and 8% for troponin and tropomyosin, respectively, compared to the values of the intact group. A similar picture is observed in the cardiac muscle.

3. Mg^{2+},Ca^{2+}-ATP-ase activity of actomyosin, starting from the 1st day, increased in both the skeletal and cardiac muscles, reaching its peak in the cardiac muscle on the 15th day, in contrast to the skeletal muscle, where this indicator reached its peak on the 7th day, and starting from the 15th day, its gradual decrease was observed; in the cardiac muscle, a slight decrease was recorded only on the 30th day, but still this indicator in both the skeletal and the cardiac muscle was greater compared to the indicator in intact animals.

4. Thus, irradiation of sexually mature animals with the dose of 0.5 Gy forms an adaptive response that is accompanied by an increase in Mg^{2+},Ca^{2+}-ATP-ase activity due to the formation of a strong form of binding between F-actin and myosin, actin monomers go into the typical for actomyosin “turned on stage”, and the myosin heads acquire an ordered orientation in the muscle fiber. An increase in Mg^{2+},Ca^{2+}-ATP-ase activity and a decrease in K^{+}-ATP-ase activity may be associated with the predominance of AM•ADP•P*i* and AM•ADP•P*i* intermediates.

5. Characterizing the changes in the activity of the direct and reverse NAD, NADPH - malate dehydrogenase reaction, as well as the content of malate and oxaloacetate in the tissues of the studied group of animals, it should be noted that the aerobic oxidation process intensifies and the energy resources of muscle tissue increase.

6. A slight increase in the content of ATP and AMP in cardiac and skeletal muscles is observed, and the concentration of ADP in these muscles is insignificantly reduced compared to non-irradiated rats. As a result, during exercise in animals irradiated with the dose of 0.5 Gy, physical performance increases by almost 10% compared to the intact group.

7. The data obtained indicated the benefit and reasonability of using in post-radiation dysfunctions complex pharmacological treatment drugs that are able to normalize intracellular homeostasis, eliminate probable acidic changes initiated by radiation exposure, activate the processes of intramuscle energy generation and which have protective properties in relation to the muscular system.

References

1. Hroza VI. Radiobiology: course of lectures. Mykolaiv: MNAU. 2018: 103. [In Ukrainian].

2. Hryban HP. Living activities and motor activity of students Zhytomyr: Ruta. 2009: 593 [In Ukrainian].

3. Lapovets LE, Lebed GB, Yastremska OO. Clinical laboratory diagnostics. Kyiv: Medicine. 2019: 472 [In Ukrainian].

4. Mardashko OO, Popyk GS, Storchilo OV. A method of correcting the homeostasis of an organism affected by radiation damage. Declaration patent of Ukraine for an invention. (11) 68126 A; 46. – 15.07.2004.

5. Medynska KO, Nuryshchenko NYe, Peliukh LI, Sheliuk OV. ATP-ase activity of the actomyosin complex of rabbit skeletal muscles under the influence of ultrasound. Ukrainian biochemical journal. 2012; 84 (4): 54-60. [In Ukrainian]

6. Baynes J, Dominiczak M. Medical Biochemistry. Glasgow : Elsevier. 2021: 744.

7. Byrne RT, Klingele AJ, Cabot EL, Schackwitz WS, Martin JA, Martin J. et al. Evolution of extreme resistance to ionizing radiation via genetic adaptation of DNA repair. Elife. 2014; 3: e01322. doi: 10.7554/eLife.01322.

8. Coleman CN. The radiation stress response: of the people, by the people and for the people. Radiat Res. 2017; 187(2): 129-146.

9. Gietl C. Malate dehydrogenase isoenzymes: cellular locations and role in the flow of metabolites between the cytoplasm and cell organelles. Biochim Biophys Acta. 1992; 1100(3): 217-34.

10. Kodali ST, Kauffman P, Kotha SR, Yenigalla A, Veeraraghavan R, Pannu SR. et al. Oxidative Lipidomics: Analysis of Oxidized Lipids and Lipid Peroxidation in Biological Systems with Relevance to Health and Disease. In: Measuring Oxidants and Oxidative Stress in Biological Systems. Cham: Springer. 2020. Chapter 5.

11. Loganovsky K, Marazziti D. Mental health and neuropsychiatric aftermath 35 years after the Chernobyl catastrophe: current state and future perspectives. Clin Neuropsychiatry. 2021; 18(2): 101-106.

12. Moroz VM, Shandra OA, Vastyanov RS, Yoltukhivsky MV, Omelchenko OD. Physiology. Vinnytsia : Nova Knyha, 2016: 722.

13. Nussbaum RH. The Chernobyl nuclear catastrophe: unacknowledged health detriment. Environ Health Perspect. 2007; 115(5): 238-239.

14. Stepanov GF. Pathophysiological mechanisms of adaptation of muscle tissue of descendants of irradiated animals to altering influence of ionizing radiation. Journal of Education, Health and Sport. 2023;48(1):225-242.

15. Stepanov GF, Vastyanov RS. The peculiarities of low-dose ionizing radiation influence on muscles metabolism in experimental animals. World of Medicine and Biology. 2023; 2(84): 233-238

16. Stepanov GF, Vastyanov RS. Involvement of intramuscular pathology at the level of the actomyosin junction into the pathogenetic mechanisms of muscle dysfunctionsin the descendents of irradiated rats. World of Medicine and Biology. 2023; 3(85): 230-236.

17. Stepanov GF, Vastyanov RS. Experimental background for hormone-vitamin complex using in course of rehabilitation after ionizing radiation. Wiadomości Lekarskie Medical Advances. 2023; 76(11): 2509-2515.

18. Stepanov GF, Vastyanov RS, Kostina AA, Lazor NV. ATPase activity of actomyosin and myosin in different types of muscles of intact and irradiated animals. Journal of Education, Health and Sport. 2023; 42(1): 161-173.

19. Stepanov GF, Vastyanov RS, Tertyshnyi SV, Petruk LH. The impact of hormone-vitamin complex on functional activity of the muscle tissue of descendants of irradiated animals. Wiadomości Lekarskie Medical Advances. 2023; 76(10): 2288-2294.

Author Contributions

Conceptualization, (Vastyanov R.S.); methodology, (Stepanov H.F.); formal analysis, (Dubna Ye.S.); data curation, (Dubna Ye.S.); writing—original draft preparation, (Mokriienko E.M.); writing—review and editing, (Stepanov H.F. & Mokriienko E.M.); supervision (Stepanov H.F. & Vastyanov R.S.). All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Institutional Review Board Statement

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 approved by the Ethics Committee of Odesa National Medical University (N7/21, 11 October 2021)

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 authors declare no conflict of interest.