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Changes in the content and activity of muscle proteins as a marker in the case of exposure to ionizing radiation in animals

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Objective. To find out the specifics of muscle tissue contraction under the conditions of exposure to low doses of ionizing radiation in parents and their irradiated offspring by evaluating changes in the content of contractile proteins and ATPase activity of skeletal and cardiac muscles. Methods. Experimental studies were conducted on 50 rats. Animals were randomized as follows: group 1 — intact sexually mature rats; 2 — sexually mature animals irradiated with a dose of 1.0 Gy; group 3 — month-old rats obtained from intact individuals; group 4 — month-old rat pups obtained from parents irradiated with a dose of 1.0 Gy; group 5 — month-old rats obtained from animals irradiated with a dose of 1.0 Gy, which were irradiated at the same dose. The results. Muscle dysfunction in irradiated offspring and parents is manifested by a decrease in the content of contractile proteins, functional dysfunction of the actomyosin bridge, and a decrease in the ATPase activity of contractile proteins. Marked muscle dysfunctions during the post-radiation time period may be the reason for the formation of orthopedic pathology in a significant contingent of irradiated persons. Conclusions. The expression of muscle dysfunction in the offspring of irradiated animals, which were also exposed to ionizing radiation, is greater than the corresponding processes in their irradiated parents, which indicates the mediation of muscle dysfunction in the second generation of irradiated animals by epigenetic mechanisms. Marked muscle dysfunctions during the post-radiation time period may be the reason for the formation of orthopedic pathology in a significant contingent of irradiated persons.

Мета. З'ясувати особливості скорочення м'язової тканини за умов впливу малих доз іонізуючого опромінення в батьків та їхніх опромінених нащадків шляхом оцінювання зміни вмісту скоротливих білків та АТР-азної активності скелетного й серцевого м'язів. Методи. Експериментальні дослідження проведено на 50 щурах. Рандомізацію тварин здійснювали наступним чином: група 1 — інтактні статевозрілі щури; 2 — статевозрілі тварини, опромінені дозою 1,0 Гр; група 3 — місячні щурята, отримані від інтактних особин; група 4 — місячні щурята, отримані від батьків, опромінених дозою 1,0 Гр; група 5 — місячні щурята, отримані від тварин, опромінених дозою 1,0 Гр, яких опромінювали в тій самій дозі. Результати. М'язова дисфункція в опромінених як нащадків, так і батьків проявляється зменшенням вмісту скоротливих протеїнів, функціональною дисфункцією акто-міозинового містка, зменшенням АТР-азної активності скоротливих білків. Відзначені м'язові дисфункції протягом післяпроменевого періоду часу можуть бути причиною формування ортопедичної патології в значного контингенту опромінених осіб. Висновки. Вираженість м'язової дисфункції в нащадків опромінених тварин, які також підпали під вплив іонізуючого опромінення, є більшою за порівняння з відповідними процесами в їхніх опромінених батьків, що свідчить про опосередкування м'язової дисфункції у другому поколінні опромінених тварин епігенетичними механізмами. Відзначені м'язові дисфункції протягом післяпроменевого періоду часу можуть бути причиною формування ортопедичної патології в значного контингенту опромінених осіб. Ключові слова. Скелетний та серцевий м'язи, іонізуюче опромінення, нащадки опромінених тварин, м'язова дисфункція, патогенетичні механізми.

Keywords. Skeletal and cardiac muscle, ionizing radiation, irradiated descendents, contractile proteins, ATPase activity of actomyosin and myosin, muscle dysfunction, pathogenetic mechanisms

Introduction

Muscle tissue is one of the four tissues of the human body that performs significant functions, it is the framework that surrounds all bones and keeps them in the right direction and location [1]. Taking into account the scale (the total mass of muscles has been proven to be equal to more than 40 % of the body mass) and prevalence in the structure of internal organs, it becomes clear its decisive role not only in ensuring the verticalization of the human body and its movement in space, but also in the regulation of functional activity vital organs and systems [1, 2].

Due to these reasons, muscle dysfunctions adversely affect the functioning of the entire body, as well as dynamic changes in pressure and direction of the location of the bones to which they are attached [3]. In this aspect, our attention was drawn to the chronic effect of a small dose of ionizing radiation on human muscles, since this problem has appeared since the accident at the Chernobyl nuclear power plant in 1986 and has gained maximum relevance now, when during military aggression against our country the use of chemical weapons by the enemy is quite possible [4–8]. Another additional component of the study is incomplete ideas about the epigenetic mechanisms of the formation of muscle disorders, since there are descendants of people who were exposed to ionizing radiation in 1986 at a fertile age. Currently, the mechanisms of induction and maintenance of radiation-induced instability of the genome in offspring remain incompletely understood. There are publications that indicate both the role of direct DNA damage and the effect on genetic instability of altered cellular metabolism.

Study of the impact of ionizing radiation on metabolism in muscle tissue is considered by a number of researchers [4, 9]. It was found that general irradiation of rats with doses of 0.5–4.5 Gy causes irreversible and dose-independent changes: edematous degeneration, intracellular lysis, damage to mitochondria of myocardial endotheliocytes, which may play a role in the development of deterministic, non-stochastic effects of radiation in small doses.

Since muscle function directly depends on the energy received as a result of oxidative metabolism reactions, firstly, the course of these reactions is disrupted due to the influence of ionizing radiation, and, secondly, energy deficit significantly changes the functional activity of actomyosin bridges, articulation of contractile muscle proteins, which by the mechanism of positive feedback initiates at least the development of pathological dysfunction of organs and systems of the body [10, 11].

The main functional characteristic of actomyosin is ATPase activity. The process of muscle contraction is associated with the formation of the actomyosin complex and its subsequent conformational changes due to the energy released because of the enzymatic splitting of ATP by myosin. Such activity of actomyosin is such a characteristic of it, by which one can judge the ability of muscles to contract. 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.

Actomyosin is characterized by Mg^{2+}-ATP-ase activity, and actually Mg^{2+}-ATP is a substrate actomyosin ATPase. In the presence of Ca^{2+}, this activity increases. In the absence of divalent cations, which is achieved by adding EDTA to the solution, myosin ATPase is activated by monovalent cations K^{+}, NH^{4+}, Rb^{+}. This activity of myosin was called EDTA-ATP-ase or K^{+}-ATP-ase activity. Monovalent cations reduce myosin's ability to bind ATP and therefore contraction is less activated. K^{+}-ATP-ase activity is a relaxing ATP-ase activity in the absence of divalent cations. The rate of the K^{+}-ATPase reaction is limited at the stage of ATP binding (much weaker than in the case of divalent cations) [2, 12].

With this in mind, the determination of the content of contractile muscle proteins, the work of which determines the functional activity of skeletal and cardiac muscles, and ATPase activity, which highlights the ability to split ATP molecules, releasing at the same time the energy necessary to ensure the contractile activity of muscles [1, 13], we consider to be the leading criteria, the study of which is important under the conditions of exposure to small doses of ionizing radiation.

Purpose: to find out the specifics of muscle tissue contraction under the influence of low doses of ionizing radiation in parents and their irradiated offspring by evaluating changes in the content of contractile proteins and ATP-ase activity of skeletal and cardiac muscles.

Material and methods

Experimental studies were conducted on 50 sexually mature Wistar white rats kept on a standard vivarium diet. Keeping, processing and manipulation of animals was carried out in accordance with the "General Ethical Principles of Animal Experiments" adopted by the Fifth National Congress on Bioethics (Kyiv, 2013), while being guided by the recommendations of the European Convention for

the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg, 1985), the methodological recommendations of the State Center of the Ministry of Health of Ukraine "Preclinical studies of drugs" (2001) and the rules of humane treatment of experimental animals and conditions approved by the bioethics commission of the Odessa National Medical University (Protocol No. 32D dated 17.03.2016).

To conduct the experiment, sexually mature rats were exposed to a single total gamma irradiation of 60Co in the morning on an empty stomach using the Agat telegammatherapy unit, the distance to the absorption source was 75 cm, the dose rate was 0.54 Gy/min, the absorbed dose was 0.5 Gy; 1.0 Gr. For irradiation, the animals were placed in a special chamber made of organic glass, size 20 × 20 × 6 cm, separated by partitions according to the size of the animals. Parents were placed in the ratio of 1 male to 5 females. The offspring of irradiated animals were not separated by sex. The experiments were conducted on the basis of the Odesa Regional Oncology Dispensary during August-September 2016, in accordance with the agreement on scientific cooperation between Odessa National Medical University and Communal Enterprise "Odesa Regional Oncology Dispensary" dated 01.04.2016.

Randomization of animals was carried out as follows: group 1 — intact sexually mature individuals; group 2 — sexually mature rats irradiated with a dose of 1.0 Gy; group 3 — month-old rats obtained from intact animals; group 4 — month-old rat pups born from parents irradiated with a dose of 1.0 Gy; group 5 — month-old rats obtained from animals irradiated with a dose of 1.0 Gy, exposed to irradiation with the same dose. There were 10 rats in all groups at the beginning of the study.

Animals were removed from the experiment by euthanasia under propofol (IV, 60 mg/kg) anesthesia. After their autopsy, blood was collected, the heart (2/3 of its top) and the front group of thigh muscles (mainly quadriceps and tetanus) were removed.

Actin, myosin, troponin, and tropomyosin were isolated from skeletal and cardiac muscles of rats at a temperature of 4 °C according to the Pardee method with minor modifications [14]. The purity of contractile proteins was assessed using denaturing polyacrylamide gel electrophoresis with sodium dodecyl sulfate in 10 % separation medium according to the method proposed by Laemmli [15].

The ATPase activity of actomyosin and myosin was determined by the amount of inorganic phosphate (Pi) formed as a result of ATP hydrolysis, according to the Fiske-Subbarow method [16].

The obtained data were subjected to statistical processing using mean "T-tables" analysis with the χ^2 criterion and computer software. The minimum statistical probability was defined as $p < 0.05$.

Results

Irradiation of sexually mature animals with a dose of 1.0 Gy leads to a significant decrease in the content of contractile proteins in skeletal and cardiac muscles. The content of such proteins in these muscles decreases with increasing time after exposure to radiation, reaching the lowest value on the 15th day compared to this indicator in intact animals (Table 1).

Assessment of the Mg^{2+}, Ca^{2+}-ATP-ase activity of actomyosin in sexually mature animals irradiated with a dose of 1.0 Gy showed that one day after the procedure, this indicator in skeletal muscle rose slightly, and then, as the time after irradiation increased, it decreased, reaching minimum value on the 30th day. In the heart muscle, a sharp increase in activity was observed on the 1st day and its decrease by the 30th day, but at the same time it remained greater than in intact animals ($p < 0.05$; Table 2).

A slight decrease in K^+-ATP-ase activity of actomyosin in skeletal muscle was proved on the 1st day of the experiment, on the 3rd day there was a slight increase compared to this indicator in intact animals. Then, with increasing time after irradiation, this activity gradually decreased, but still exceeded these data compared to intact animals, in contrast to heart muscle, where actomyosin K^+-ATPase activity with increasing time after irradiation gradually decreased and reached its lowest value on the 30th day compared to this indicator in intact animals ($p < 0.05$).

Significant changes in the functioning of muscle tissue occurred in rat pups born from irradiated with a dose of 1.0 Gy, exposed to radiation at the same dose. A decrease in the content of contractile proteins in skeletal and cardiac muscles was observed in offspring born from sexually mature animals irradiated with a dose of 1.0 Gy compared to the corresponding indicators in intact rat pups ($p < 0.05$; Table 3).

One day after irradiation with a dose of 1.0 Gy, offspring born from sexually mature animals irradiated with the same dose showed a tendency to decrease the content of contractile proteins in skeletal and cardiac muscles compared to intact rats, especially the content of troponin and tropomyosin in skeletal muscle liver, the content of which was probably lower than the similar indicators of intact rats by 2 and 2.6 times, respectively, and tropomyosin in

heart muscle, where this indicator was probably lower by more than 2 times ($p < 0.05$).

With increasing time after irradiation, the content of contractile proteins sharply decreased in both skeletal and cardiac muscles compared to intact rats and reached its peak decrease on the 30th day after exposure to radiation, where the content of myosin in skeletal muscle was lower by almost 2.5 times, but not likely, the content of actin — 9 times, troponin — 7.3 times, and tropomyosin — 7 times, which was significantly less compared to the corresponding values in intact rats ($p < 0.05$).

In the heart muscle, the content of actin was almost 2.3 times lower, troponin — 6.8 times, and tropomyosin — 8.5 times, which was less compared to the corresponding values in intact rats, in contrast to myosin ($p < 0$ .05), the content of which was almost 45 % lower, which slightly differed from this indicator in intact rat pups.

After irradiation with a dose of 1.0 Gy of rat pups born from animals irradiated with the same dose, with increasing time after exposure, the activity of Mg^{2+}, Ca^{2+}-ATP-ase of actomyosin and myosin and K^{+}-ATP-ase of actomyosin and myosin in all types of muscle decreases muscles, reaching the lowest values on the 30th day, where in skeletal muscle Mg^{2+}, Ca^{2+}-ATP-ase activity of actomyosin and myosin is 2.2 and 2.8 times lower, respectively, compared to intact animals, and K^{+}-ATP-ase activity of actomyosin and myosin — 1.6 and 2 times, respectively ($p < 0.05$; Table 4).

In the heart muscle on the 30th day after irradiation, the K^{+}-ATPase activity of actomyosin and myosin was 1.5 times lower compared to intact animals,

Table 1

Time course of the content of contractile proteins in skeletal and cardiac muscles of sexually mature rats irradiated with a dose of 1.0 Gy

Protein under the study	Location (muscle)	The content of contractile proteins in rat muscles after exposure to ionizing radiation, M ± m, (μmol per 1 g of tissue)					
		intact, n = 10	1 day, n = 10	3 days, n = 10	7 days, n = 9	15 days, n = 8	30 days, n = 7
Myosin	Skeletal	8.9 ± 5.7	7.7 ± 5.6	7.2 ± 5.5	7.0 ± 5.5	6.5 ± 5.5	6.6 ± 5.5
	Cardiac	9.7 ± 5.9	8.8 ± 5.8	8.5 ± 5.8	8.1 ± 5.7	7.8 ± 5.6	8.2 ± 5.7
Actin	Skeletal	4.0 ± 0.4	3.5 ± 0.4	3.2 ± 0.3	3.0 ± 0.3	2.6 ± 0.2	2.8 ± 0.3
	Cardiac	4.5 ± 0.4	4.2 ± 0.4	4.1 ± 0.4	4.0 ± 0.4	3.7 ± 0.3	4.0 ± 0.4
Troponin	Skeletal	1.7 ± 0.2	1.5 ± 0.2	1.3 ± 0.2	1.1 ± 0.2	0.8 ± 0.1	1.0 ± 0.1
	Cardiac	1.8 ± 0.2	1.7 ± 0.2	1.4 ± 0.2	1.2 ± 0.1	1.0 ± 0.1	1.3 ± 0.1
Tropomyosin	Skeletal	1.8 ± 0.2	1.7 ± 0.2	1.4 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	1.0 ± 0.1
	Cardiac	2.0 ± 0.2	1.7 ± 0.2	1.6 ± 0.2	1.3 ± 0.2	1.1 ± 0.2	1.3 ± 0.2

Table 2

ATPase activity of actomyosin and myosin in skeletal and cardiac muscles of sexually mature rats irradiated with a dose of 1.0 Gy

Protein under the study	Location (muscle)	ATPase activity of actomyosin and myosin in rat muscles after exposure to ionizing radiation, M ± m, (nmol Pi/min per mg of protein)					
		intact, n = 10	1 day, n = 10	3 days, n = 10	7 days, n = 9	15 days, n = 8	30 days, n = 7
Mg^{2+}, Ca^{2+}-ATP-ase activity of actomyosin	Skeletal	96.50 ± 11.32	98.80 ± 11.74	92.90 ± 11.62	92.30 ± 11.56	91.80 ± 11.54	90.70 ± 11.52
	Cardiac	108.80 ± 10.66	129.20 ± 10.94	118.60 ± 10.72	119.40 ± 10.68	126.80 ± 10.56	116.40 ± 10.54 *
K^{+}-ATPase activity of actomyosin	Skeletal	17.80 ± 2.76	16.80 ± 3.25	18.60 ± 3.22	17.40 ± 3.18	17.90 ± 3.14	17.30 ± 3.12
	Cardiac	24.80 ± 3.16	21.80 ± 3.14	20.40 ± 3.12	20.20 ± 3.18	20.80 ± 3.16	20.20 ± 3.16
Mg^{2+}, Ca^{2+}-ATPase activity of myosin	Skeletal	104.20 ± 8.52	101.40 ± 8.46	99.20 ± 8.38	98.30 ± 8.24	96.80 ± 8.22	98.60 ± 8.25
	Cardiac	116.90 ± 6.84	118.60 ± 6.84	110.20 ± 6.68	104.60 ± 6.56	102.40 ± 6.48	100.80 ± 6.34
K^{+}-ATPase activity of myosin	Skeletal	50.60 ± 3.26	50.60 ± 3.25	66.84 ± 3.92 *	64.38 ± 3.86 *	62.52 ± 3.84 *	60.86 ± 3.72
	Cardiac	52.88 ± 3.30	60.26 ± 4.24	68.48 ± 4.22 *	74.46 ± 4.18 *	72.32 ± 4.16 *	70.84 ± 4.14 *

Note. * — $p < 0.05$ — probable discrepancies of the studied indicators compared to the corresponding indicators in intact animals.

and the Mg^{2+},Ca^{2+}-ATPase activity of actomyosin and myosin was 1.8 and 2.1 times, respectively ($p < 0.05$).

Discussion

Therefore, the given data indicate damage to skeletal and cardiac muscles as a result of the impact of ionizing radiation with a dose of 1.0 Gy, manifested by modification of the functional unit of muscle contraction — the actomyosin protein complex. The disproportion of contractile muscle proteins determines a change in the functional activity of actomyosin joints and causes an increase in the K^+-ATPase activity of actomyosin in radiation-sensitive muscles.

In the case of ionizing radiation with a dose of 1.0 Gy on pure myosin, a decrease in Mg^{2+}, Ca^{2+}-ATP-ase activity of myosin in skeletal muscle was recorded throughout the entire post-irradiation period of observation. In the heart muscle, a wave-like

Table 3

Time course of the content of contractile proteins in skeletal and cardiac muscles of offspring born from sexually mature animals irradiated with a dose of 1.0 Gy, exposed to the same dose

Protein under the study	Location (muscle)	The content of contractile proteins in rat muscles after exposure to ionizing radiation, M ± m, (μmol per 1 g of tissue)						
		intact, n = 10	born from irradiated, n = 10	1 day, n = 10	3 days, n = 10	7 days, n = 9	15 days, n = 8	30 days, n = 7
Myosin	Skeletal	4.9 ± 2.6	3.4 ± 2.2	3.1 ± 2.2	2.9 ± 2.3	2.6 ± 1.9	2.3 ± 1.8	2.0 ± 1.3
	Cardiac	5.2 ± 2.7	4.7 ± 2.3	4.4 ± 2.2	3.9 ± 2.2	3.5 ± 2.1	3.2 ± 2.0	2.9 ± 1.8
Actin	Skeletal	2.0 ± 0.4	1.2 ± 0.2	1.1 ± 0.2	0.8 ± 0.2 [1]	0.7 ± 0.1 [1]	0.5 ± 0.1 [1, 2]	0.2 ± 0.1 [1, 2]
	Cardiac	2.8 ± 0.3	2.3 ± 0.2	2.1 ± 0.2	2.0 ± 0.2	2.0 ± 0.2	1.5 ± 0.1 [1]	1.2 ± 0.1 [1, 2]
Troponin	Skeletal	0.9 ± 0.1	0.6 ± 0.1	0.4 ± 0.1 [1]	0.3 ± 0.1 [1]	0.21 ± 0.04 [1, 2]	0.26 ± 0.04 [1, 2]	0.12 ± 0.02 [1, 2]
	Cardiac	1.0 ± 0.2	0.7 ± 0.1	0.6 ± 0.1	0.4 ± 0.1 [1]	0.3 ± 0.1 [1, 2]	0.22 ± 0.04 [1, 2]	0.14 ± 0.02 [1, 2]
Tropomyosin	Skeletal	1.0 ± 0.1	0.5 ± 0.1	0.4 ± 0.1 [1]	0.3 ± 0.1 [1]	0.24 ± 0.04 [1]	0.18 ± 0.04 [1, 2]	0.14 ± 0.02 [1, 2]
	Cardiac	1.0 ± 0.2	0.7 ± 0.2	0.5 ± 0.1 [1]	0.3 ± 0.1 [1]	0.26 ± 0.04 [1, 2]	0.18 ± 0.02 [1, 2]	0.12 ± 0.02 [1, 2]

Notes: [1] — $p < 0.05$ — probable discrepancies of the investigated indicators compared to the corresponding indicators in intact animals; [2] — $p < 0.05$ — probable discrepancies of the investigated indicators compared to such indicators in non-irradiated animals.

Table 4

ATP-ase activity of actomyosin and myosin in skeletal and cardiac muscles of offspring born from sexually mature animals irradiated with a dose of 1.0 Gy, exposed to a dose of 1.0 Gy

Protein under the study	Location (muscle)	ATPase activity of actomyosin and myosin in rat muscles after exposure to ionizing radiation, M ± m, (nmol Pi/min per mg of protein)						
		intact, n = 10	born from irradiated, n = 10	1 day, n = 10	3 days, n = 10	7 days, n = 9	15 days, n = 8	30 days, n = 7
Mg^{2+}, Ca^{2+}-ATP-ase activity of actomyosin	Skeletal	93.54 ± 8.32	84.80 ± 8.26	80.60 ± 8.22	72.60 ± 8.14	65.30 ± 7.64 [1]	58.60 ± 5.84 [1, 2]	42.40 ± 5.12 [1, 2]
	Cardiac	108.20 ± 10.64	98.40 ± 9.86	92.60 ± 9.24	86.80 ± 8.72	82.40 ± 8.56	74.80 ± 7.72 [1]	60.80 ± 6.14 [1, 2]
K^+-ATPase activity of actomyosin	Skeletal	17.20 ± 2.76	14.70 ± 2.24	18.80 ± 2.72	18.20 ± 2.68	16.60 ± 2.62	15.40 ± 2.14	10.60 ± 1.38
	Cardiac	24.30 ± 3.16	22.30 ± 3.12	25.20 ± 3.68	26.80 ± 3.84	24.60 ± 3.24	20.80 ± 2.96	16.40 ± 2.62
Mg^{2+}, Ca^{2+}-ATPase activity of myosin	Skeletal	102.30 ± 6.52	88.20 ± 6.26	84.60 ± 6.24	76.20 ± 5.88 [1]	62.80 ± 5.44 [1, 2]	52.80 ± 5.26 [1, 2]	36.20 ± 4.58 [1, 2]
	Cardiac	116.40 ± 6.86	100.90 ± 6.68	90.60 ± 5.52 [1]	84.40 ± 5.26 [1]	79.60 ± 4.98 [1, 2]	70.20 ± 4.12 [1, 2]	56.40 ± 3.76 [1, 2]
K^+-ATPase activity of myosin	Skeletal	50.40 ± 3.26	42.60 ± 3.18	46.80 ± 3.22	47.40 ± 3.24	40.80 ± 2.86 [1]	32.60 ± 2.48 [1, 2]	24.80 ± 2.12 [1, 2]
	Cardiac	52.76 ± 3.28	46.34 ± 3.32	47.96 ± 3.64	48.72 ± 3.86	45.68 ± 3.26	38.24 ± 2.86 [1]	34.86 ± 2.52 [1, 2]

Notes: [1] — $p < 0.05$ — probable discrepancies of the investigated indicators compared to the corresponding indicators in intact animals; [2] — $p < 0.05$ — probable discrepancies of the investigated indicators compared to such indicators in non-irradiated animals.

change in the activity of the studied indicator was observed: an increase on the 1st day and a further decrease with increasing time after irradiation. We assume that the decrease in Mg^{2+}, Ca^{2+}-ATP-ase activity of myosin may be due to a violation of the structure of its active center, since the ATP-ase center of pure myosin is directly free from interaction with actin, and that is why myosin is more sensitive to the action of ionizing radiation.

It is interesting that the K^{+}-ATP-ase activity of myosin in cardiac and skeletal muscles always increased after irradiation, reaching its maximum value on the 7th day, and starting from the 15th, a tendency to decrease this indicator was observed.

Comparing the obtained data on the effect of ionizing radiation on the general ATP-ase activity, the following mechanism of influence on the actomyosin complex can be assumed. A decrease in ATP-ase activity under the conditions of action of ionizing radiation on the muscles of the body occurs due to the formation of a weak form of binding of myosin to actin (the AM•ATP and AM•ADP•Pi stage), disorientation of the myosin heads develops, and actin monomers pass into "off state". The functional weakness of the muscle system under the specified conditions is explained by the dysfunction of the actomyosin complex, which results in insufficient coupling of the heads of actin, myosin and functional deficiency of troponin and tropomyosin. Due to this, the muscle weakness of the skeletal and cardiac muscles, which developed as a result of irradiation, can be corrected under the influence of a complex scheme of pharmacological drugs that are able to normalize the energy resource of the muscles.

Another interesting block of the obtained results is data on changes in the content of contractile proteins and changes in ATP-ase activity in the offspring of irradiated rats, which themselves were exposed to ionizing radiation with a dose of 1.0 Gy. Summarizing the obtained results, we note that in the offspring of animals irradiated with a dose of 1.0 Gy, which were exposed to radiation at the same dose, there are significant changes in the functioning of muscle tissue, manifested by a sharp decrease in the content of contractile proteins. If we compare these indicators with the data in the offspring of intact rats, it should be noted that irradiation sharply reduces the adaptive capabilities of the organism of the offspring of animals irradiated with a dose of 1.0 Gy, after exposure to radiation.

In addition, in the muscle tissue of irradiated rats born from animals irradiated with a dose of 1.0 Gy, there was a significant decrease in Mg^{2+}, Ca^{2+}-ATP-ase activity of actomyosin and myosin and K^{+}-ATP-ase activity of actomyosin and myosin, which was the result of impaired fixation of these enzymes by tissues. And if we consider that during irradiation with a dose of 1.0 Gy, tissue respiration is suppressed, then with an increase in the dose, we should expect more significant disturbances in the bioenergetics of muscles, especially cardiac ones, since the dominant way of replenishing ATP in it is tissue respiration and the associated phosphorylation, while in skeletal — glycolysis.

Studies conducted to clarify the mechanism of the effect of ionizing radiation with a dose of 0.5 Gy on the functioning of skeletal and cardiac muscles revealed minor changes in the content of contractile proteins and almost no ATP-ase activity, which was, for the most part, a consequence of the adaptive variant of the muscle response system to the action of a stress factor of insignificant intensity [17]. Under these conditions, most likely, biosynthetic processes are stimulated, increasing the adaptive capabilities of the body, which can be explained by the phenomenon of hormesis [18, 19].

Therefore, an irradiation dose of 1.0 Gy, which is insignificant for the initiation of pronounced changes in the muscles of irradiated subjects, in case of repeated exposure to the next generation, is a sufficient and necessary model stimulus that provides an opportunity to study the peculiarities of changes in muscle characteristics in time course of the post-radiation period. According to the fundamental mechanisms, the heart muscle is known to have a greater risk of developing muscle dysfunction under the specified model conditions, since the consequence of energy deficit is more pronounced in it. This is confirmed by the higher content of mitochondria in cardiac muscle compared to skeletal muscle [1, 13]. It is in the mitochondria that intensively function the processes of tissue respiration, which provide the myocardium with a higher content of ATP, unlike skeletal muscle, where the ATP pool is replenished mainly by the glycolytic pathway [13]. Therefore, stimulation of mitochondrial energy processes, according to our results, is another recommendation regarding the scheme of complex pathogenetically oriented treatment of post-radiation muscular dysfermentoses.

In summary, we note that the severity of muscle dysfunction in the offspring of irradiated animals, which were also exposed to ionizing radiation, was greater than the corresponding processes in their parents, indicating that muscle dysfunction in the second generation of irradiated animals was mediated by epigenetic mechanisms. Muscle dysfunction in

irradiated offspring of irradiated parents was manifested by a decrease in the content of contractile proteins, functional dysfunction of the actomyosin bridge, a decrease in the ATP-ase activity of contractile proteins, which generally indicates a pronounced energy deficit, which makes the process of effective rapid muscle contraction impossible. Marked muscle dysfunctions during the post-radiation period of time can be the reason for the formation of orthopedic impairment in a significant contingent of irradiated subjects, if we are talking about skeletal muscle. And in the case of a predominant damage to the heart muscle, the signs of heart failure and the pathological dysfunction of organs and systems initiated by it should be expected and prevented [20]. We consider the given set of actual results as an experimental justification for the feasibility of pharmacological correction of energetic muscle deficit in irradiated persons, which has a pathogenetic basis and is a method of prevention of musculoskeletal disorders.

Conclusions

The expression of muscle dysfunction in the offspring of irradiated animals, which were also exposed to ionizing radiation, is greater when compared with the corresponding processes in their irradiated parents, indicating the mediation of muscle dysfunction in the second generation of irradiated animals by epigenetic mechanisms.

Marked muscle dysfunctions during the post-radiation period may be the reason for the formation of orthopedic impairment in a significant contingent of irradiated subjects.

We consider the given set of actual results as an experimental justification for the feasibility of pharmacological correction of energetic muscle deficit in irradiated persons, which has a pathogenetic basis and is a method of prevention of musculoskeletal disorders.

Conflict of interest. The authors declare no conflict ofinterest.

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CHANGES IN THE CONTENT AND ACTIVITY OF MUSCLE PROTEINS AS A MARKER IN THE CASE OF EXPOSURE TO IONIZING RADIATION IN ANIMALS

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