WL Layout 10 2023

Article · October 2023

CITATIONS
0

READS
373

4 authors, including:

Serhii Tertyshnyi
military medical clinical center of the southern region
48 PUBLICATIONS **14** CITATIONS
SEE PROFILE

Gennadiy Stepanov
Odessa National Medical University
9 PUBLICATIONS **3** CITATIONS
SEE PROFILE

Liubov Petruk
Одесский национальный медицинский университет
9 PUBLICATIONS **4** CITATIONS
SEE PROFILE

Wiadomości Lekarskie
Medical Advances

VOLUME LXXVI, ISSUE 10, OCTOBER 2023
Official journal of Polish Medical Association has been published since 1928

ISSN 0043-5147
E-ISSN 2719-342X

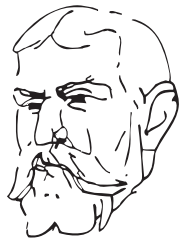
INDEXED IN PUBMED/MEDLINE, SCOPUS, EMBASE, EBSCO, INDEX COPERNICUS,
POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

Wiadomości Lekarskie
Medical Advances

VOLUME LXXVI, ISSUES 10, OCTOBER 2023
Official journal of Polish Medical Association has been published since 1928

ISSN 0043-5147
E-ISSN 2719-342X

ALUNA Publishing



Memory of
dr Władysław
Biegański

Wiadomości Lekarskie is abstracted and indexed in: PUBMED/MEDLINE, SCOPUS, EMBASE, INDEX COPERNICUS, POLISH MINISTRY OF EDUCATION AND SCIENCE, POLISH MEDICAL BIBLIOGRAPHY

The journal Wiadomości Lekarskie is cofinanced under Contract No.RCN/SN/0714/2021/1 by the funds of the Minister of Education and Science

Wiadomości Lekarskie
Medical Advances

Distribution and Subscriptions:
Bartosz Guterman prenumerata@wydawnictwo-aluna.pl
Graphic design / production:
Grzegorz Sztank fajne.work

Publisher:
ALUNA Publishing
ul. Przesmyckiego 29,
05-510 Konstancin – Jeziorna
www.wydawnictwo-aluna.pl
www.wiadomoscilekarskie.pl
www.wiadlek.pl

ORIGINAL ARTICLE

THE IMPACT OF HORMONE-VITAMIN COMPLEX ON FUNCTIONAL ACTIVITY OF THE MUSCLE TISSUE OF DESCENDANTS OF IRRADIATED ANIMALS

DOI: 10.36740/WLek202310125

Gennadiy F. Stepanov, Rooslan S. Vastyanov, Serhii V. Tertyshnyi, Lyubov H. Petruk
ODESA NATIONAL MEDICAL UNIVERSITY, ODESA, UKRAINE

ABSTRACT

The aim: To determine the hormone-vitamin complex impact on the terminal links of glycolysis, the tricarboxylic acids cycle, and the initial stage of gluconeogenesis in the muscle tissue in descendants of irradiated animals.

Materials and methods: Pyruvate kinase, lactate dehydrogenase, malate dehydrogenase, NADP-dependent malate dehydrogenasee and phosphoenolpyruvate carboxykinase activities, the content of lactate, pyruvate, malate and oxaloacetate were determined in the blood, myocardium and thigh muscles of 66 rats after exposure to ionizing gamma-radiation. Rats were injected by a hormone-vitamin complex which efficacy was determined using the abovementioned indexes.

Results: Hormone-vitamin complex administration to descendants of irradiated animals exposed to 1.0 Gy results to pyruvate kinase activity increase in the myocardium and skeletal muscles of descendants from animals irradiated by 0.5 Gy and exposed to 1.0 Gy irradiation.

Blood serum pyruvate kinase activity in descendants from animals irradiated by 1.0 Gy and exposed to 1.0 Gy radiation after the pharmacological correction was higher compared with the same index before pharmacological correction.

The lactate dehydrogenase activity in the myocardium, skeletal muscles and blood in descendants born from animals irradiated by maximal dose exposed to 1.0 Gy radiation was less in these tissues after pharmacological correction.

Conclusions: The hormone-vitamin complex use in the descendants of irradiated animals led to muscle tissue energy resources improvement. Our data are the experimental background for theoriginal hormone-vitamin complex efficacy further evaluation in the aspect of vital organs and body systems functional activity restoration under the influence of ionizing radiation.

KEY WORDS: total irradiation, descendants of irradiated animals, physical working capacity, hormone-vitamin complex, mechanisms of development

Wiad Lek. 2023;76(10):2288-2294

INTRODUCTION

The problem of the biological effect of ionizing radiation, especially in small doses, and protection against it continues to be one of the fundamental problems in the of medical and biological sciences complex in Ukraine [1-3]. The impact of ionizing radiation on the body causes destructive changes that occur at all structural and functional levels of the organization [4-6].

The general state of the body after the effects of ionizing radiation and the changes caused by this radiation largely determine the functioning of muscle tissue [7-10], which plays an important role in ensuring the vital activity of the body, and considering that the descendants of irradiated animals are exposed to physical stress, deeper biochemical changes in the metabolism of muscle tissue should be expected [9]. Of particular importance is the substrate phosphorylation enzymes failure, which plays a leading role in bioenergetics, the weakening of the function of NAD-dependent dehydrogenases of the tricarboxylic acid cycle and the lipid peroxidation intensification which results to biomembranes both structure and function failure [11]. In addition, catabolic processes leading to protein destruction and negative nitrogen balance are enhanced [12].

One of the real ways to improve the health of the population can be the use of agents that have antioxidant properties that increase the body's resistance to adverse factors [13, 14]. The results of previously conducted research and the analysis of data from the scientific literature prove the effectiveness of separate use of anabolic steroid drugs [15], vitamin E [16] and other vitamins [17], in particular, as radioprotective compounds that have protective effects, including increasing of the lifespan of experimental animals. The original idea was the joint introduction of the above-mentioned pharmacological compounds to

test their effectiveness in the descendants of irradiated animals [18].

THE AIM

The aim was to determine the hormone-vitamin complex impact on the terminal links of glycolysis, the tricarboxylic acids cycle and the initial stage of gluconeogenesis in the muscle tissue in descendants of irradiated animals.

MATERIALS AND METHODS

Experimental studies were carried out on 66 mature white Wistar 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). We used the recommendations of the European Convention on the Protection of Vertebrate Animals for Experimental and Other Scientific Purposes (Strasbourg, 1985) 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 03/17/2016).

The mature rats were exposed to a single total gamma irradiation of ^{60}Co in the morning on an empty stomach on the "Agat" telegammatherapy unit (the distance to the device was 75 cm, the dose rate was 0.54 Gy/min, the absorbed dose was 0.5 Gy and 1.0 Gy).

The animals were randomized in the following way: the 1st group (n=10) – 1-month-old rats born from intact animals; the 2nd and the 3rd groups (n=2x10) – 1-month-old rat pups born from animals once totally irradiated by 0.5 Gy and 1.0 Gy; the 4th and the 5th groups (n=2x10) – 1-month-old rat pups born from animals once totally irradiated by 0.5 Gy and by 1.0 Gy and exposed to a dose of 1.0 Gy; the 6th and the 7th groups (n=2x8) – 1-month-old rat pups born from animals once totally irradiated by 0.5 Gy and by 1.0 Gy and exposed to a dose of 1.0 Gy, which were administered with a hormone-vitamin complex (HVC).

The HVC included tocopherol acetate (i.m., 50 mg/kg, 30 min after irradiation), retabolil (i.m., 2.5 mg/kg, 3 hrs after irradiation), cocarboxylase (s.c., 5 mg /kg) and nicotinamide (s.c., 10 mg/kg), which were administered 1 day after irradiation dissolved in 0.5 ml of saline. The HVC was administered during 12 days [18].

After euthanasia (i.v., propofol, 60 mg/kg) the animals' blood was collected, the heart (2/3 of the heart`s apex) and the frontal group of thigh muscles (mainly quadriceps femoris and sartorius muscle) were removed. Blood was centrifuged at 3000 g for 10 min to obtain serum. The removed cardiac and skeletal muscles were washed with chilled 0.9% physiological NaCl solution, minced and homogenized and subjected to differential centrifugation in a refrigerated centrifuge PC-6.

To detect the biosubstrates content in tissues, they were immersed in liquid nitrogen, deproteinized with 0.6N perchloric acid and homogenized. The protein precipitate was separated by centrifugation for 15 min at 3000 g.

Mitochondria, mitochondrial supernatant of myocardium, thigh muscles frontal group and blood serum were used for biochemical studies. We determined the activity of pyruvate kinase (PK), lactate dehydrogenase (LDH), malate dehydrogenase (MDH), NADP-dependent MDH, phosphoenolpyruvate carboxykinase and the content of lactate, pyruvate, malate, and oxaloacetate [19].

PK activity was determined according to [20] and expressed in μmoles of pyruvate per mg of protein in the sample for 1 min of incubation. LDH activity was determined according to [19] and expressed in nmol of used $NADH+H^+$ per mg of protein in the sample for 1 min of incubation.

MDH activity was determined according to [19] and expressed in μmol of formed NADH per mg of protein in the sample in 1 min. incubation The activity of phosphoenolpyruvate carboxy kinase was determined according to [21] and expressed in nmol of oxidized NADH per mg of protein in the sample for 1 min of incubation.

The content of lactate, pyruvate, malate, and oxaloacetate was determined according to [19] and expressed in μmol per 1 g of tissue and in nmol per 1 g of tissue (for oxaloacetate).

The data obtained were presented as mean (x) and the standard error of the mean (SE). $\chi 2$ criterion was used to detect the significant differences between the investigated groups $p<0.05$ was considered asa statistically significant difference.

RESULTS

The HVC administration to irradiated descendants, which were exposed to a dose of 1.0 Gy, leads to PK activity increase in the myocardium and skeletal muscles of the descendants born from animals once irradiated by 0.5 Gy and exposed to irradiation in a dose of 1.0 g. These indexes are increased by 6.7% in cardiac and 10.9% in skeletal muscles compared to such data in rats that did not receive HVC (in both cases $p>0.05$).

In the muscle tissue of descendants born from animals irradiated at a dose of 1.0 Gy and exposed to irradiation at the same dose, PK activity is reduced. The PK activity is greater by 15.5% and by 21% in cardiac and skeletal

Table I. The influence of the hormone-vitamin complex on the activity of NAD-dependent malatedehydrogenases and the content of reaction metabolites in the tissues of 1-month-old rats born from irradiated animals and exposed to radiation at a dose of 1.0 Gy

N	Enzymes and metabolites	Myocardium		Skeletal muscle		Blood
		Cytoplasm	Mitochondria	Cytoplasm	Mitochondria	
Intact rat pups (the 1st group), n=10						
1	NAD-MDH (direct reaction)	0.582±0.052	0.286±0.023	0.214±0.014	47,37±3,24	1,932±0,164
2	NAD-MDH (reverse reaction)	2.461±0.021	0.216±0.032	1.065±0.026	54,18±3,61	4,372±0,362
3	Malat	0.336±0.029		0.118±0.011		0.107±0.011
4	Oxaloacet	47.43±3.17		39.18±2.84		15.72±1.32
1-month-old rats born from animals once irradiated by 0.5 Gy and exposed to irradiation at a dose of 1.0 Gy (the 4th group), n=10						
Before correction						
1	NAD-MDH (direct reaction)	0.656±0.18	0.236±0.014	0.278±0.008	40,36±2,80	2,244±0,198
2	NAD-MDH (reverse reaction)	2.464±0.152	0.268±0.054	1.448±0.074*	68,24±2,92	4,618±0,314
3	Malat	0.389±0.024		0.164±0.013		0.117±0.014
4	Oxaloacet	43.76±2.75		36.19±2.65		14.82±1.33
After correction						
1	NAD-MDH (direct reaction)	0.632±0.18	0.226±0.01	0.264±0.008	43,28±3,20	1,786±0,178
2	NAD-MDH (reverse reaction)	2.084±0.144	0.248±0.056	1.284±0.056	66,48±2,86	4,282±0,312
3	Malat	0.392±0.026		0.172±0.014		0.124±0.012
4	Oxaloacet	42.68±1.96		34.52±1.74		14.48±1.26
1-month-old rats born from animals once irradiated by 1.0 Gy and exposed to irradiation at a dose of 1.0 Gy (the 5th group), n=10						
Before correction						
1	NAD-MDH (direct reaction)	0.984±0.36	0.178±0.012*	0.314±0.012*	26,56±1,4*	1,246±0,134*
2	NAD-MDH (reverse reaction)	3.814±0.236*	0.296±0.088	1.838±0.096*	78,52±3,64*	5,722±0,386*
3	Malat	0.492±0.084		0.236±0.022*		0.184±0.016*
4	Oxaloacet	59.12±3.96*		55.06±3.48*		19.24±2.16
After correction						
1	NAD-MDH (direct reaction)	0.686±0.20#	0.254±0.016	0.278±0.008	41,94±3,2#	1,924±0,186#
2	NAD-MDH (reverse reaction)	1.998±0.134#	0.278±0.072	1.296±0.068	68,42±2,92	4,546±0,342
3	Malat	0.416±0.032		0.178±0.016		0.128±0.014
4	Oxaloacet	43.62±1.94		35.84±1.76#		15.94±1.28

Notes: group numbers correspond to those given in "Materials and Methods" * - $p<0.05$ - significant differences of the investigated indexes compared with the same in intact rat pups; # - $p<0.05$ – significant differences of the investigated indexes compared with the same before correction.

muscles, respectively, compared to similar data in animals that did not receive HVC ($p>0.05$). The activity of this enzyme is significantly lower in blood serum of descendants born from animals irradiated at a dose of 0.5 Gy and exposed to radiation at a dose of 1.0 Gy ($p<0.05$), and its increase by 1.5 times is observed in the blood serum of descendants born from animals irradiated at a dose of 1.0 Gy and exposed to irradiation at the same dose, to which HVC was administered ($p<0.05$).

The activity of LDH in the myocardium, skeletal muscles and blood of descendants born from animals irradiated with the maximal dose, which were exposed to radiation at a dose of 1.0 Gy, after the HVC injection is characterized by a significant decrease in activity ($p<0.05$).

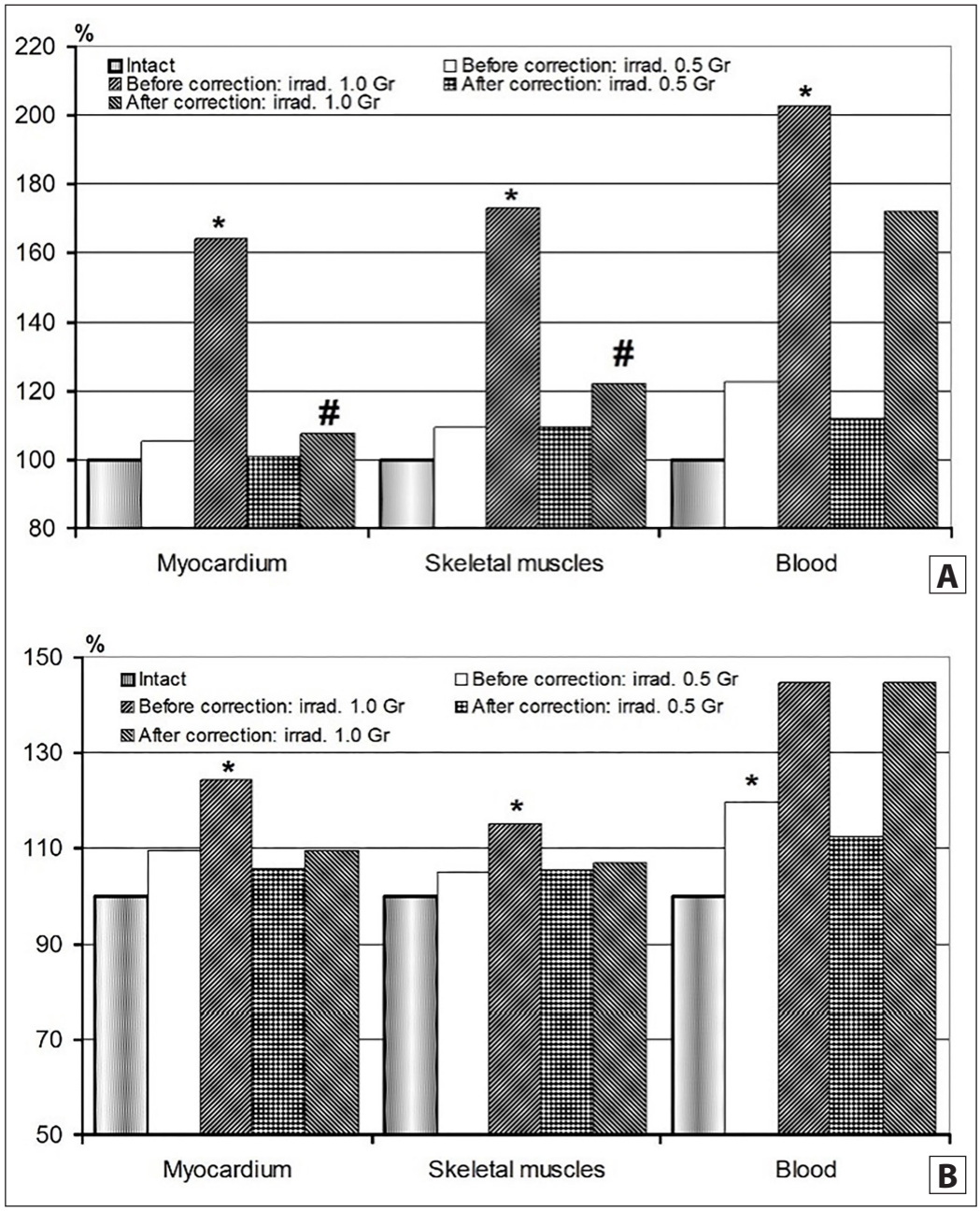


Fig. 1. The influence of the hormone-vitamin complex on the content of glycolysis metabolites (lactate; appendix A); (pyruvate; appendix B) in the investigated tissues of 1-month-old rats born from irradiated animals and exposed to radiation at a dose of 1.0 Gy.
Notes: * - $p<0.05$ – significant differences of the investigated indexes compared with the same in intact rat pups; # - $p<0.05$ – significant differences of the investigated indexes compared with the same before correction.

The pharmacological correction prevents the increase of phosphoenolpyruvate carboxykinase activity in the tissues of irradiated descendants exposed to radiation at a dose of 1.0 Gy.

The pyruvate and lactate content in the investigated tissues of irradiated descendants, which were exposed to radiation at a dose of 1.0 Gy, after the HVC introduction has some parallelism with the same indexes in the same descendants which did not receive HVC therapy ($p>0.05$; Fig. 1).

A slight increase in lactate content was observed in the myocardium and skeletal muscle of 1-month-old rats born from animals once irradiated by 0.5 Gy and exposed to irradiation at a dose of 1.0 Gy after the HVC injection (Fig. 1, A). A more pronounced increase in lactate content in muscle tissue of irradiated descendants by 1.0 Gy and exposed to irradiation at a dose of 1.0 Gy ($p<0.05$). The content of lactate in the blood of the studied rats also exceeds the same control index, and a significantly higher lactate concentration is observed in the blood of irradiated descendants by 1.0 Gy and exposed to irradiation at a dose of 1.0 Gy ($p<0.05$).

The pyruvate content after the HVC introduction exceeds the same index both in the muscle tissue and blood of 1-month-old rats born from animals irradiated by 0.5 Gy and exposed to irradiation at a dose of 1.0 Gy, as well as in all the investigated tissues of descendants born from irradiated animals by of 1.0 Gy and exposed to radiation at a dose of 1.0 Gy ($p>0.05$; Fig. 1, B).).

The activity of NAD-dependent MDH in the cytoplasm of cardiac and skeletal muscles of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HCV injection is comparable to the corresponding control index. The activity of the direct NAD-dependent MDH reaction in the mitochondria of cardiac and skeletal muscles of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HVC introduction is reduced, and the lowest values are observed in rats born from animals irradiated at a dose of 1.0 Gy and exposed to irradiation at a dose of 1.0 Gy, however, these indexes are identical to the same in intact rats ($p>0.05$; Table I).

The activity of the direct NAD-dependent MDH reaction in the blood of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HVC introduction also reduced, and the lowest index is observed in rats born from irradiated animals by 0,5 Gy exposed to radiation at a dose of 1.0 Gy ($p>0.05$).

The activity of NAD-dependent MDH in the myocardium cytoplasm of irradiated descendants exposed to radiation with a dose of 1.0 Gy after the HVC introduction is lower compared to the intact group, and the lowest indicator of its activity is observed in the cytoplasm of the myocardium in rats born from animals irradiated by 1.0 Gy and exposed to irradiation at a dose of 1.0 Gy after PMC introduction ($p>0.05$).

The activity of NAD-dependent MDH (reverse reaction) in the mitochondria of cardiac and skeletal muscles, as well as in the blood of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HVC introduction is comparable to same control indexes ($p>0.05$).

The malate and oxaloacetate content in the muscle tissue and blood of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HVC introduction has a multidirectional nature. Against the background of a slightly increased concentration of malate in muscle tissue and blood, the content of oxaloacetate decreases compared to intact rats. As a result, an increase in the ratio of malate to oxaloacetate was observed in the examined tissues of irradiated descendants exposed to radiation at a dose of 1.0 Gy after the HVC introduction compared to irradiated descendants exposed to radiation in a dose of 1.0 Gy which did not receive pharmacological correction.

DISCUSSION

Thus, the obtained results indicate that the HVC introduction to the irradiated of animals, exposed to radiation at a dose of 1.0 Gy, led to an energy resources improvement in muscle tissue both due to the increase in glycolytic substrate phosphorylation, which is of dominant importance for providing energy to skeletal muscles, and due to the increase in the oxidative potential of the tricarboxylic acid cycle not only at the stage of MDH action, but also at the stage that is catalyzed by succinatedehydrogenase. We consider it appropriate to stress the following ideas.

Firstly, we assumed that the pharmacological correction of radiation disorders of energy metabolism in irradiated descendants exposed to radiation at the same doses should be aimed at correcting disorders by the tissues provision with macroergic compounds that occur according to catabolism prevailing over anabolism, anaerobic processes strengthening, metabolic acidosis development in tissues, weakening of substrate phosphorylation and the cycle of tricarboxylic acids, as well as cellular genetic apparatus damage prevention, regeneration processes normalization [4, 11].

Secondly, we suppose to understand the mechanisms of the radioprotective effect realization in the used corrective pharmacological scheme: the improvement of lactate and pyruvate accumulation as the end products of glycolysis in the tissues of the descendants, the weakening of the processes of substrate and oxidative phosphorylation, which leads to malate and oxaloacetate - the final products of the tricarboxylic acid cycle - increase. It is important to understand that in the accumulation of malate, the leading role is played by the activation of the reverse NAD-dependent MDG in the cytoplasm and in the mitochondria of muscle tissue, as well as the predominance of the reverse NADP-dependent MDH reaction, which ensures the pyruvate carboxylation and its transformation into malate [11, 22].

Finally, let us add that glycolytic substrate phosphorylation is of dominant importance for providing energy to skeletal muscles, therefore, based on the results obtained, it can be stated that under the influence of the hormone-vitamin complex, the energy resources of skeletal muscles are improved, which will definitely be reflected in the physical performance of the descendants, born from irradiated animals and exposed to radiation at the same dose [9, 11, 23].

Therefore, the increase in malate and oxaloacetate content in the muscle tissue and blood in the irradiated descendants exposed to radiation by 1.0 Gy after the HVC introduction, according to our ideas, occurs due to malate content increase in both tissues and the oxaloacetate content decrease. Thus, we can talk about

the increase of the oxidation potential of the cycle of tricarboxylic acids not only at the MDG stage but also at the stage catalyzed by succinate dehydrogenase.

CONCLUSIONS

1. Pronounced radioprotective efficacy of the HVC, which includes tocopherol, retabolil, cocarboxylase, and nicotinamide, was proved for the normalizing energy processes in the muscle tissue of the irradiated animals descendants.
2. The radioprotective efficacy of the applied HVC consisted in blood PK activity normalization, LDH muscle tissue, and blood activity normalization as well as in preventing an increase of phosphoenolpyruvate carboxykinase activity in the examined tissues of the irradiated animals descendants.
3. Under the influence of the hormone-vitamin complex, a decrease in the content of lactate in cardiac and skeletal muscles was noted, which improved the energy resources of the muscle tissue of the irradiated animals descendants.

REFERENCES

1. Azarov SI, Eremenko SA, Sydorenko VL et al. Tekhnohenno-ekolohichni naslidky Chornobylskoi katastrofy [Technogenic and ecological consequences of the Chernobyl disaster]. Kyiv: MPBP Hordon. 2019, p.455. (in Ukrainian).
2. Andrushkiv B. Nekhtuvannia problemamy Chornobylskoi trahedii ye naslidkovym lantsiuhom vynyknennia suchasnykh problem povnomasshtabnoi viiny z Rosiieiu [Neglecting the problems of the Chernobyl tragedy is a consequential chain of the emergence of modern problems of a full-scale war with Russia]. Naukovo-informatsiinyi visnyk Natsionalnoi akademii nauk vyshchoi osvity Ukrainy. 2022; 1: 13-18. (in Ukrainian).
3. Buzunov VO, Krasnikova LI, Voychulene YS et al. Epidemiolohichni doslidzhennia kardio- ta tserebrovaskulyarnykh zakhvoriuvan v uchasnykiv likvidatsii naslidkiv avarii na chornobylskii AES: Analiz vplyvu radiatsiinoho i neradiatsiinykh faktoriv [Epidemiological studies of cardiovascular and cerebrovascular diseases in participants in liquidation of the consequences of the accident at the Chernobyl nuclear power plant: Analysis of the influence of radiation and non-radiation factors]. Zhurnal NAMN Ukrainy. 2016; 22(2): 153-162. (in Ukrainian).
4. Burgio E, Piscitelli P, Migliore L. Ionizing Radiation and Human Health: Reviewing Models of Exposure and Mechanisms of Cellular Damage. An Epigenetic Perspective. International journal of environmental research and public health. 2018; 15(9): 1971. doi:10.3390/ijerph15091971.
5. Helm JS, Rudel RA. Adverse outcome pathways for ionizing radiation and breast cancer involve direct and indirect DNA damage, oxidative stress, inflammation, genomic instability, and interaction with hormonal regulation of the breast. Archives of toxicology. 2020; 94(5): 1511-1549. doi:10.1007/s00204-020-02752-z.
6. Shivappa P, Bernhardt GV. Natural Radioprotectors on Current and Future Perspectives: A Mini-Review. Journal of pharmacy & bioallied sciences. 2022; 14(2): 57-71. doi:10.4103/jpbs.jpbs_502_21.
7. Fedirko P, Pilmane M, Babenko TF, Konopecka V. Holovnyi mozok ta orhan zoru yak potentsiini misheni dlia vplyvu ionizuiuchoho vyprominiuvannia. Chastyna IV – Rozlady binokuliarnoho zoru ploda, sprychyneni radiatsiinym vplyvom in utero: pilotne doslidzhennia. imunohistokhimichni zminy neoprominenykh miaziv ochnoho yabluka pry kosookosti. mozhlyvyi mekhanizm rozvytku kosokosti v osib, yaki zaznaly prenatalnoho oprominennia [Brain and eye as potential targets for ionizing radiation impact. Part IV - fetal radiation-induced binocular vision disorders: a pilot study. Immunohistochemical changes of non/irradiated eyeball muscles affected by strabismus. Evidence of a possible mechanism of the strabismus development in persons exposed to fetal radiation]. Problemy radiatsiinoi medytsyny ta radiobiolohii/ Problems of radiation medicine and radiobiology. 2022; 27: 412-422. doi:10.33145/2304-8336-2022-27-412-422. (in Ukrainian).
8. Lumniczky K, Impens N, Armengol G et al. Low dose ionizing radiation effects on the immune system. Environment international. 2021; 149: 106212. doi:10.1016/j.envint.2020.106212.
9. Paithankar JG, Gupta SC, Sharma A. Therapeutic potential of low dose ionizing radiation against cancer, dementia, and diabetes: evidences from epidemiological, clinical, and preclinical studies. Molecular biology reports. 2023;50(3):2823-2834. doi:10.1007/s11033-022-08211-5.
10. Xu P, Yi Y, Luo Y et al. Radiation-induced dysfunction of energy metabolism in the heart results in the fibrosis of cardiac tissues. Molecular medicine reports. 2021;24(6):842. doi:10.3892/mmr.2021.12482.
11. Baynes J, Dominiczak M. Medical Biochemistry. Elsevier; 2023, p. 744.
12. Bondar OI, Vashchenko VM, Azarov SI et al. Chornobyl chetverte desiatylittia [Chernobyl in the fourth decade]. Kyiv: NAIR. 2019, p. 407 (in Ukrainian).
13. Levchenko OE. Viiskova toksykolohiia, radiolohiia, medychnyi zakhyst [Military toxicology, radiology, medical protection]. Kyiv: SPD Chalchynska N.V. 2017, p. 361 (in Ukrainian).
14. Azzam EI, Colangelo NW, Domogauer JD et al. Is Ionizing Radiation Harmful at any Exposure? An Echo That Continues to Vibrate. Health physics. 2016;110(3):249-251. doi:10.1097/HP.0000000000000450.

15. Yamaguchi M, Suzuki M, Funaba M et al. Mitigative efficacy of the clinical dosage administration of granulocyte colony-stimulating factor and romiplostim in mice with severe acute radiation syndrome. Stem cell research & therapy. 2020;11(1):339. doi:10.1186/s13287-020-01861-x.
16. Nukala U, Thakkar S, Krager KJ et al. Antioxidant Tocols as Radiation Countermeasures (Challenges to be Addressed to Use Tocols as Radiation Countermeasures in Humans). Antioxidants (Basel, Switzerland). 2018;7(2):33. doi:10.3390/antiox7020033.
17. Lledó I, Ibáñez B, Melero A et al. Vitamins and Radioprotective Effect: A Review. Antioxidants (Basel, Switzerland). 2023;12(3):611. doi:10.3390/antiox12030611.
18. Mardashko OO, Popyk GS, Storchilo OV. Sposib korektsii homeostazu orhanizmu, yakyi zaznav vplyvu radiatsiinoho urazhennia [A method of correcting the homeostasis of an organism affected by radiation damage]. Ukraine Patent UA 68126. 2004. https://sis.ukrpatent.org/uk/search/detail/378445/ [date access 08.04.2023] (in Ukrainian0
19. Lapovets LE, Lebed GB, Yastremska OO. Klinichna laboratorna diahnostyka [Clinical laboratory diagnostics]. Kyiv: Medytsyna; 2019, p. 472. (in Ukrainian).
20. Nakonechna OA, Bachynskyi RO. Biokhimiia fermentiv. Aspekty medychnoi enzymolohii [Biochemistry of enzymes. Aspects of medical enzymology]. Kharkiv. 2020, p. 48. (in Ukrainian).
21. Fulghum KL, Audam TN, Lorkiewicz PK et al. In vivo deep network tracing reveals phosphofructokinase-mediated coordination of biosynthetic pathway activity in the myocardium. Journal of molecular and cellular cardiology. 2022;162:32-42. doi:10.1016/j.yjmcc.2021.08.013.
22. Fix DK, Hardee JP, Bateman TA, Carson JA. Effect of irradiation on Akt signaling in atrophying skeletal muscle. Journal of applied physiology. 2016;121(4):917-924. doi:10.1152/japplphysiol.00218.2016.
23. 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. doi:10.26724/2079-8334-2023-2-84-233-238.

Source of funding: within the framework of the scientific target program "Mechanisms of epigenetic disorders of the leading links of bioenergetics and nitrogen metabolism in irradiated animals and their descendants" of the Ministry of Health of Ukraine (state registration No. 0121U114601; 2021-2026).

ORCID and contributionship:
Gennadiy F. Stepanov: 0000-0002-8242-8689 [A-D]
Rooslan S. Vastyanov: 0000-0001-8585-2517 [C,E,F]
Serhii V. Tertyshnyi: 0000-0002-4949-5409 [C,D,F]
Lyubov H. Petruk: 0000-0002-1261-7054 [C,E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Gennadiy F. Stepanov
Odesa National Medical University
2 Valikhovsky lane, 65082 Odesa, Ukraine
tel: +380679948948
e-mail: medchem@ukr.net

Received: 09.04.2023
Accepted: 17.09.2023

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article