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Ergoprotective Effect of Vitamins in Toxic Liver Damage

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Abstract: The introduction of hepatotropic poisons into the body of experimental rats in combination with starvation and hypothermia at the first stages increases physical performance. However, continued exposure to these factors leads to a significant decrease in performance and the development of splenocytes with inhibitory properties. The use of vitamins A and B1 separately helps to normalize performance, and their combined use neutralizes the effects of hepatotropic poisons, affecting splenocytes. Vitamins A, E, and C create a pronounced neuroprotective effect, and their combination with thiamine, carotene, and biotin improves the physical activity of rats during starvation and hypothermia. This effect is enhanced by the addition of polyunsaturated phospholipids (for example, essentiale).

Keywords: vitamins that support energy and antioxidant, hepatotropic poisons, geroprotective effect, efficiency, polyunsaturated phospholipids.

The study of metabolic disorders associated with various disorders of oxidative energy homeostasis has shown that all of them lead to a decrease in physical performance. Movement is the main manifestation of an organism's vital activity. In the process of evolution, it has become an important element of homeostasis, ensuring the interaction of the body with the external environment. Homeostasis associated with muscle activity is necessary to maintain the overall balance of the body at rest. At the whole body level, movement plays a key role in the functioning of the cardiovascular, respiratory, digestive, and immune systems. Limiting physical activity under stress and various diseases leads to impaired metabolism and functional processes, which makes it difficult for the body to adapt to adverse environmental conditions. Increasing the ability to perform physical activity is an important condition for the prevention and treatment of many diseases.

A decrease in physical activity and working capacity is associated with a violation of the balance of oxidative-energetic processes, which disrupts the structure and functions of cell membranes. When xenobiotics enter the body, their main part is absorbed by hepatocytes. The liver is the main organ through which food, medicinal and toxic substances enter the bloodstream. Hepatocytes are constantly exposed to chemical irritants, which causes changes in the activity of enzymatic systems, as well as the formation and release of various substances into the blood that affect vital body processes. The liver plays a key role in regulating the immune system and non-specific body defenses. It synthesizes substances such as creatine phosphate, glucose and ketone bodies, which are necessary for the functioning of muscle tissue. Disorders in the liver can lead to disruptions in its connection with other body systems, which is one of the reasons for the development of various pathologies. The introduction of toxic substances can cause a deficiency of vitamins necessary for proper muscle function (A, E, B1, B5, B6, B9).

Based on this, it can be assumed that vitamins with antioxidant properties and energizing activity, especially in combination with membranotropic substances, can be effective means for correcting motor functions in various disorders of homeostasis. **The purpose** of this study was to study the effect of hepatotropic poisons on physical performance and to evaluate the possibility of its correction with the help of vitamins with antioxidant and energizing properties. **Materials and research methods** The experiments were conducted on Wistar rats with a body weight of 160-180 g. Animals were injected ten times with CCL4 at a dose of 2 ml per 100 g of body weight once a day with an interval of 24 hours or D-galactosamine (D-HA) at a dose of 0.5 ml per 100 g of body weight according to the same scheme. During this period, the rats did not receive food, but had free access to water. The animals were cooled using water at a temperature of 10 °C for 5 hours. The duration of the experiment was 15 days. Vitamin preparations were administered intramuscularly to rats: A (10 mg/kg), E (20 mg/kg), C (30 mg/kg), as well as thiamine (2 mg/kg), carnitine (5 mg/kg), biotin (3 mg/kg). Essentiale was administered intravenously at a dose of 10 mg/kg. The drugs were used daily during the entire follow-up period. The occurrence of toxic hepatitis was judged by the increased activity of aspartate and alanine aminotransferase (AST and ALT), alkaline phosphatase (ALP) and total bilirubin (AB) in blood plasma, as well as the concentration of diene conjugates (DC) and malonic dialdehyde (MDA) in liver homogenate. The content of 2,3-bisphosphoglycerate (BPH) and adenosine triphosphate (ATP) in red blood cells was used to assess the state of energy metabolism. A violation of protein-synthetic liver function was detected by a decrease in protein concentration in blood plasma.

Physical performance was assessed by the maximum duration of swimming at a water temperature of 25± 10 °C with a load of 8% of body weight (high-intensity physical activity) or 20% of body weight (submaximal intensity physical activity).

Serum donors were rats that received poisoning and vitamins, serum was isolated from the blood 4 hours after the last administration of CCL4 and administered three times with an interval of 24 hours, 0.5 ml per 100 g of body weight. Splenocytes were obtained by squeezing cells from the crushed mass of the organ and washed with medium 199, after which they were suspended in 0.15 M NaCl and injected intravenously into intact animals with 107 cells in a volume of 0.2 ml. Splenocytes were incubated in sterile siliconized tubes for 4 hours at a temperature of 37 ° C, resuspending every 30 minutes. After incubation, the cells were deposited by centrifugation. Splenocytes of intact rats were incubated with the serum of animals poisoned with CCL4 for 3 hours at 37 °C. After incubation, the cells were washed with medium 199 and suspended again in 0.15 M NaCl, after which they were injected into rats receiving vitamins. Statistical data processing was performed using methods of variational statistical analysis and calculation of averages and standard error using Microsoft Excel 2010 software. To assess the significance of the differences, the Student's t-test was used; at $p<0.05$, the results were considered statistically significant.

Results: Tenfold administration of CCL4 led to a decrease in physical performance at both high and submaximal intensity. Vitamins A and B1, administered separately to poisoned animals, improved performance, but did not restore it completely. The greatest ergoprotective effect was observed with the administration of vitamin B1. With the combined use of vitamins A and B1, it was possible to normalize the performance of high and submaximal intensity physical activity. After CCL4 administration, transaminase activity increased in the blood of animals, while the AST/ALT ratio remained below 1. Levels of BPH and ATP decreased in red blood cells, and concentrations of DC and MDA increased in the liver. The level of protein in the blood plasma of the poisoned rats did not change compared with the control. Blood serum from poisoned animals reduced physical performance in intact rats. The introduction of vitamin A prevented the accumulation of substances in the serum that reduced performance. Vitamin B1 had no such effect. Blood serum from CCL4-poisoned animals reduced physical performance in rats treated with vitamin A. However, rats treated with vitamin B1 showed resistance to the action of serum from poisoned animals.

Table 1. The effect of vitamins A and B1 on the physical performance of rats poisoned with hepatotropic poison

Terms of the experience	Swimming with a load of 8% of body weight	Swimming with a load of 20% of body weight
Intact animals that did not receive vitamins	12,6±0,9	3,1±0,4
Animals poisoned with CCL4 that did not receive vitamins	3,2±0,3*	1,0±0,2*
Poisoned animals receiving vitamin A	7,3±0,5*	2,9±0,3*
Poisoned animals receiving vitamin B1	5,1±0,4*	1,4±0,2*
Poisoned animals receiving vitamins A and B1	11,4±0,9*	3,4±0,3*

*Note: * – indicates the significance of the difference (p<0.05)*

Table 2. The effect of serum from poisoned rats on the physical performance of intact animals

Terms of the experience	Swimming with a load of 8% of body weight	Swimming with a load of 20% of body weight
Control (without administration of serum)	12,6±0.9	3,2±0,4
Administration of serum from intact rats that had not received hepatotropic venom and vitamins	11,9±0,8	3,0±0,3
Administration of serum from poisoned rats that did not receive vitamins	5,7±0,3*	1,7±0,1*
Administration of serum from poisoned rats treated with vitamin A	12,3±1,0*	3,8±0,4*
Administration of serum from poisoned rats to intact animals receiving vitamin A	4,2±0,3*	1,6±0,1*
Administration of serum from poisoned rats to intact animals receiving vitamin B1	4,9±0,4*	1,5±0,1*
Administration of serum from poisoned rats to intact animals receiving vitamin B1	11,7±0,9*	3,5±0,4*

*Note: * – indicates the significance of the difference (p<0.05)*

Table 3. Geroprotective effects of adherent splenocytes from intact rats treated with serum from animals poisoned with CCL4 and treated with vitamins A and B1

Experimental conditions	ANVI	FANCY
Control without splenocyte injection	12,7±0,8	3,2±0,3
Administration of splenocytes from control rats	13,2±0,9	3,6±0,3
Administration of splenocytes from rats poisoned with CCL4	6,8±0,4*1,2	1,4±0,3*1,2
Administration of splenocytes from intact rats treated with serum from intact animals	12,6±0,7*	3,4±0,4*
Administration of splenocytes from intact rats treated with serum from poisoned rats	8,4±0,5*	1,2±0,2*
Administration of splenocytes from intact rats treated with vitamin A	13,2±0,8*	4,0±0,4*
Administration of splenocytes from vitamin A-treated rats treated with serum from poisoned animals	7,8±0,5*	1,5±0,2*
Administration of splenocytes from vitamin B1-treated rats	14,1±0,9*	4,1±0,5*
Administration of splenocytes from rats receiving vitamin B1 treated with serum from poisoned animals	13,6±0,8*	3,8±0,4*

*Note: * – indicates the significance of the difference (p<0.05)*

Table 4. The effect of vitamins A, E, and C on physical performance during D-HA administration, fasting, and cooling

Experimental conditions	Introduction of D-HA	Starvation	Cooling
1. Introduction of vitamin A	4,2±0,8	4,3±0,8	3,6±1,2
2. Introduction of vitamin E	5,2±0,9	3,7±0,8	4,4±0,7
3. Introduction of vitamin C	4,5±0,7	3,9±0,6	4,0±0,8
4. Introduction of vitamins A, E and C	10,4±1,3*	8,8±1,1*	7,8±0,9*

*Note: * – indicates the significance of the difference (p<0.05)*

Discussion of the results: The observed increase in physical performance was mainly related to improvements in task performance at submaximal intensity (FNSI), while improvements in high intensity (FNVI) were less pronounced. The degree of decrease in working capacity increased with the duration of exposure to stress factors. The greatest decrease was observed during cooling for FNSI, and for FNVI — with the introduction of carbon tetrachloride.

The use of antioxidant vitamins (A, E, and C) alone did not significantly improve the ability to perform tasks at high and submaximal intensity during cooling and starvation. Nevertheless, when hepatotropic venom was administered, these vitamins contributed to an improvement in the performance of tasks at submaximal intensity (FNSI). The combined use of antioxidant vitamins significantly increased physical performance, especially in cases of toxic liver damage, although the effect was less pronounced when cooling and fasting.

The use of thiamine during cooling and fasting improved the performance of tasks at submaximal intensity (FNSI), but did not lead to a complete restoration of this ability. While thiamine, carnitine, and biotin alone did not have a noticeable effect on the performance of high-intensity exercise (HDTF), their combined use in combination with other energizing vitamins (thiamine, carnitine, biotin) significantly increased performance on both the FNSI and FNVI tests during cooling and fasting.

The use of thiamine under the influence of cooling and starvation improved the performance of tasks at submaximal intensity, but did not restore it to normal. At the same time, the combination of energizing vitamins (thiamine, carnitine, biotin) showed a more pronounced increase in performance on both tests (FNSI and FNVI) compared with injections of antioxidant vitamins under the influence of cold and hungry stress.

The introduction of D-HA, combined with starvation or cooling, caused a significant decrease in physical performance, starting from the first days of exposure to stress factors. However, this decrease could be compensated by the use of vitamin complexes containing antioxidants or energizing vitamins. The combined administration of antioxidant vitamins with polyunsaturated phospholipids led to an improvement in physical performance according to the FNSI and FNVI tests under conditions of exposure to D-HA, starvation or cooling (Table 5).

Таблица 5. The effect of essentiale on the ergoprotective activity of vitamins during fasting, combined with cooling or the introduction of D-HA

Experimental conditions		Fasting + cooling	Fasting + introduction to-	HA Cooling + introduction to-HA
1.	Introduction of vitamins A, B and C.	3,6±0,3	4,3±0,5	3,7±0,4
2.	Introduction of vitamins A, B and C + essentiale	14,8±1,3*	15,8±1,6*	12,4±1,3*
3.	Introduction of thiamine, biotin and carnitine	4,5±0,6*	4,4±1,6*2	3,9±0,5*
4.	Introduction of thiamine, biotin and carnitine + essentiale	11,6±1,2*	13,3±1,4*1	12,6±1,2*1

*Note: * – indicates the significance of the difference (p<0.05)*

The experimental results demonstrated a close structural and functional relationship between the liver, immunocompetent cells, and muscle tissue under stress and pathology. This connection is realized through chemical compounds that are secreted by hepatocytes or liver macrophages, as well as, possibly, peptides produced by macrophages of the spleen. It was previously established that there is a relationship between metabolic processes in the liver affected by toxic substances and immune functions carried out through proteolytic enzymes in the vascular bed [14]. There is reason to believe that such an enzyme mechanism may be involved in the transmission of signals from hepatocytes through immunocytes to myocytes, regulating their contractions. This hypothesis is supported by data according to which antiproteolytic proteins (such as trasilol and kontrical) significantly increase performance in rats poisoned with hepatotropic poisons [14].

The processes occurring in the liver play an important role in supporting the functions of muscle tissue. Hepatocytes synthesize glucose from amino acids and other non-carbohydrate compounds, form metabolites, which are then converted in myocytes into creatine phosphate and ketone bodies, which are used for energy supply to muscle tissue along with glucose.

With toxic liver damage, which is accompanied by starvation and cooling, there is an increase in the activity of aspartate and alanine aminotransferases (AST and ALT) in the blood, as well as an increase in the De Ritis coefficient (AST/ALT), which indicates damage to the mitochondrial membranes and the transition of metabolism to the catabolic phase. This leads to an accelerated breakdown of nitrogenous compounds and a slowdown in protein synthesis.

Toxic liver damage also reduces the amount of fat-soluble vitamins deposited in the liver, in particular vitamin A and its derivatives. Inhibition of protein biosynthesis increases the body's need for vitamins A and B1, which activate anabolic processes and energy supply to cells [17].

The research results have shown that impaired functional performance when hepatotropic venom enters the body is mostly corrected by the use of antioxidant vitamin complexes, while decreased performance during starvation and cooling is best eliminated by the introduction of energizing vitamin mixtures. This is consistent with modern concepts of a violation of the antioxidant potential caused by hepatotropic poisons and a decrease in the energy supply of cells due to a deficiency of vitamins and energy carriers during starvation and cooling [8].

Special attention is drawn to the potentiating effect of polyunsaturated phospholipids (for example, essentiale) on the effects caused by antioxidant and energizing vitamin mixtures. Enzymes that catalyze oxidative energy processes are associated with the membranes of mitochondria and the endoplasmic reticulum. In conditions of toxic hepatopathy, cooling and starvation, the structures of cell membranes are disrupted, and polyunsaturated phospholipids help to stabilize the membranes, thereby improving the energy supply of cellular processes that support the functioning of muscle cells. Polyunsaturated phospholipids have the greatest effect on the membranes of liver cells [4, 5].

These improvements in the functioning of liver cells contribute to an increase in the efficiency of muscle contractions, since hepatocytes deposit glucose, which is used by myocytes, synthesize creatine, which is converted into reserve energy material in myocytes, and also synthesize ketone bodies, which are an easily accessible source of energy for muscles [7].

The data obtained confirm that a wide range of functional activity of vitamins regulated by the state of cell membranes can become the basis for the development of multifunctional vitamin compositions, which, in combination with membrane-stabilizing compounds, can not only improve physical performance, but also adjust metabolic processes characteristic of various organs and tissues. The ingestion of hepatotropic poisons (such as CCL4 and D-HA) activates free radical processes in hepatocytes and the formation of lipid peroxidation products [17].

Lipid peroxidation products such as dienone conjugates and malondialdehydes, penetrating into myocytes, probably cause cross-oxidation of contractile proteins. Vitamin A, interacting with alkyd radicals, slows down the formation of lipid hydroperoxides and products of oxidative

degradation of hepatocyte proteins [1]. Vitamin B1, in turn, prevents the destruction of contractile proteins of myocytes, probably by activating the energy blocks of myocytes.

The decrease in physical performance due to the intake of hepatotoxic substances on the background of starvation or cooling is not corrected by the combined use of vitamins A and B1. However, the ergoprotective effect in these conditions is achieved through the use of antioxidant or energizing vitamin mixtures in combination with polyunsaturated phospholipids that stabilize cell membranes. These phospholipids have a similar effect when using both antioxidants and energizing vitamins.

Polyunsaturated phospholipids enhance the effects of vitamins of both the oxidative group (riboflavin, niacin, coenzyme Q) and the anabolic group (pyridoxine, folate, cobalamin) [2]. This allows us to consider polyunsaturated fatty phospholipid preparations as universal vitamin therapy enhancers for various forms of stress and pathology.

Based on the conducted studies, the following conclusions can be drawn:

The intake of hepatotropic CCL4 or D-HA poisons, as well as temporary starvation and cooling, increase the physical performance of rats in the first three days, but later these factors reduce performance, disrupting energy homeostasis.

Administration of vitamins A or B1 separately to poisoned rats improves their physical performance, but does not restore it completely. The combined use of vitamins A and B1 eliminates the depressing effect of hepatotropic poison on performance. The introduction of CCL4 causes the accumulation of substances in the blood of rats that reduce performance and contribute to the manifestation of ergosuppressive properties in spleen cells. Vitamin A prevents the accumulation of toxic compounds in the blood that reduce the performance of animals, and vitamin B1 increases the resistance of rats to the effects of these substances. The ergosuppressive effect of CCL4 and the ergoprotective effect of vitamins A and B1 are manifested through the involvement of spleen cells. The combined use of antioxidant vitamins (A, E, and C) has a pronounced ergoprotective effect in toxic liver damage caused by D-HA. At the same time, the introduction of energizing vitamins (thiamine, carnitine, and biotin) is significantly more effective than antioxidants in improving performance during starvation and cooling. The intake of D-HA into the body in combination with starvation or cooling causes a significant decrease in physical performance from the very first three days of exposure to the agents. This decrease is partially offset by the introduction of antioxidant or energizing vitamin complexes. The ergoprotective effect with a combination of D-HA, fasting and cooling is achieved by the introduction of antioxidant or energizing vitamin compositions in combination with polyunsaturated phospholipids (essentiale).

Bibliography:

1. Burnevich E.Z. Hepatic encephalopathy in cirrhosis of the liver /E.Z.Burnevich, T.N., M.S.Krasnova // Hepatological. forum. – 2018. – No. 2. p. 19-24.
2. Butorova L.I. Medicinal liver lesions: textbook.- methodical. manual / L.I.Butorova, A.V.Kalinin, A.F.Loginov. Moscow: Federal State University "NMHTS named after N.I. Pirogov", 2015. 65 p.
3. Vartanyan F.E. Tuberculosis: problems and scientific research in the countries of the world / F.E.Vartanyan, K.P.Shakhovsky // Problems of tuberculosis. 2002. No. 8. pp. 48-49.
4. Vasilenko Yu.K. The effect of pectoinulin and its combination with taurine on detoxifying activity of the liver / Y.K.Vasilenko [et al.] //Vestn. Russian University of Friendship of Peoples.- 2012. – No. 1. – pp. 22-26.-Ser. Medicine.
5. Vedennikova A.V. Genetic aspects of alcoholic liver disease. The results of the study / A.V.Vedennikova [et al.] // Hepatology today: tez.dokl. tenth Russian Conference– Moscow, 2005– p.57.

6. Vedrova N.N. Experience of using methadoxyl in the complex treatment of alcoholic liver damage / N.N. Vedrova, N.Yu. Gnezdilova // Narcologist.-2005.-No. 4. - pp. 24-26.
7. Vengerovsky A.I. Methodological guidelines for the study of hepatoprotective activity of pharmacological substances / A.I.Vengerovsky, I.V.Markova, A.S.Saratikov // Guidelines for the experimental (preclinical) study of new pharmacological substances / edited by V.P.Fisenko. – Moscow, 2000. – pp.228-231
8. Vengerovsky A.I. Methodological guidelines for the study of hepatoprotective activity of pharmacological substances /A.I.Vengerovsky, I.V.Markova, A.S.Saratikov//Guidelines for the experimental (preclinical) study of new pharmacological substances / edited by R.U. Khabriev. Moscow, 2005. pp.683-691.
9. Verokhobina N.V. The place of Dibikor in the treatment of patients with type 2 diabetes mellitus and metabolic syndrome /N.V.Verokhobina, A.V.Kuznetsova // Pharmateca. - 2012. – No. 3. – p.75-77