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Energetic criteria of lymphocytes in evaluation of efficacy of system processes correction under oncopathology

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Abstract

The activity of key ferments in the Krebs cycle (SDH) and glycolysis (α -GPDH) in peripheral blood lymphocytes in animals and humans with cancer pathology is considered herein. Identified is a close relationship between the fermentative activity and non-specific integral reactions of an organism, the type of which can be regulated by factors of electromagnetic nature. Monitoring of signal energetic and adaptive reactions permits to adequately evaluate an efficacy of treatment and predict recovery.

Keywords

Blood lymphocytes, Dehydrogenases, Cancerogenesis, Mammary gland cancer

Imprint

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Special attention which is paid to lymphocytes is related not only to their role as immune competent cells. Their capability to participate in regulation of a number of the organism non-immune functions from energetic and free radical processes at the catecholamine level in blood to physiological regeneration, growth and development has a great significance. Thus the lymphocyte criteria serve as a dynamic indicator which gives a new meaning to the signal structure

of basic characteristics of the organism robustness [1, 2].

According to Prof. M.N. Kondrashova, the founder of the Russian School of mitochondrial energetics, blood lymphocytes are an inspection glass in our organism, since they carry a direct signal of energetic metabolism [1, 2]. Meant is an integral change in the mitochondrial system in the organism that is adequately demonstrated by the state of lymphocyte dehydrogenases. Known is the

existence of the direct relationship between the activity of mitochondrial glycerophosphate dehydrogenase (α -GPDH) and succinate dehydrogenase (SDH) [3-5]. The relation between the activity both of α -GPDH and SDH and the immune reaction indicators is determined by the function of these ferments: α -GPDH participates in functioning of the glycerophosphate shunt which governs the glycolysis state, while SDH participates in the Krebs cycle as the key ferment. Modulation of the activity of SDH and the related α -GPDH reflects not only the type of the cell metabolism rearrangement, but the formation of qualitatively different types of adaptive reactions [6, 7] as well. Thus, under stress, the lowest indicators of SDH ($8,6 \pm 0,7$ in conventional units) and α -GPDH ($6,2 \pm 0,6$ in conventional units) activity are reported, that allows assuming there is a disorder in the integration of the processes of phosphorylating respiration and glycolysis. Besides, a reduction in the macroerg production in lymphocytes leads to a disorder in permeability and intactness of cell membranes and organelles that is dangerous for highly sensitive systems like the nervous and cardiovascular ones. Under development of the reaction of activation, a much more higher activity of SDH ($15,1 \pm 2,0$; $p < 0,001$) and α -GPDH ($8,8 \pm 0,4$; $p < 0,05$) has been recorded as compared to that under the stress conditions that demonstrates a good energy availability of lymphocytes. The activity of the lymphocyte dehydrogenases under development of the reaction of training has been reported to be lower than that under the reaction of activation (SDH $12,5 \pm 2,6$ and α -GPDH $7,2 \pm 0,8$), but higher than that under stress [6, 7]. It proves that the activity of the lymphocyte

dehydrogenases in peripheral blood can determine a degree of damage or restoration not only at the level of the immune system cell components, but also at the level of the organism with its discreteness of the states of the norm and pathology [8, 9].

Disorders in mitochondrial processes with a deficiency of the SDH activity are observed for a great variety of nosological forms from cardiovascular diseases to insufficiency of gastric secretion and renal function. R.P. Nartsissov [10] considers that the cytochemical analysis of the peripheral blood lymphocytes is a “mediated biopsy” of viscera. For instance, the state of a SDH depression is typical for severe pathology in newborns and serves as a predictor of their further development. The most advanced computer-aided medical diagnostics systems include calculations of energetic parameters in cardiometry [11, 12].

Despite the fact that the ferment systems of lymphocytes under different system disorders are well studied, research on the ferment activity of lymphocytes in case of development and treatment of malignant tumors under applications of some factors of regulatory influence remains of topical significance.

An evaluation of the activity of the lymphocyte dehydrogenases in peripheral blood under experimental conditions of the tumor growth and medication of the mammary gland cancer with the use of an electromagnetic field exposure has become the aim of the study described herein.

Some experiments have been carried out by modeling chemically induced cancerogenesis in 72 albino rats. Brain scanning with the use of very low frequency magnetic field (VLF MF) has been carried out ac-

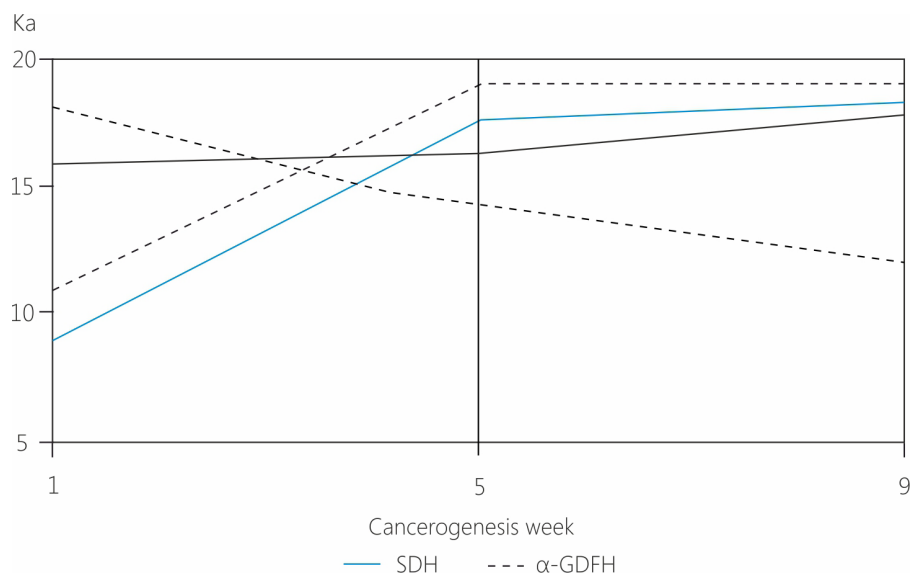


Figure 1. Change in activity of dehydrogenases of lymphocytes in peripheral blood in rats at early stages of cancerogenesis for reference group versus VLF MF exposed group (thick lines)

cording to the algorithm of frequencies of 0,03-0,3-3-9 Hz with rectangular impulse modulation of 300 Hz, at the 3.2mT induction and 8 min. exposure [13].

An application of VLF MF during week 1 of cancerogenesis significantly retarded a reduction of the ferment activity of the peripheral blood lymphocytes as compared to the reference values. A balance in the operation of the SDH-α-GPDH system reflected a coordinated interaction between the Krebs cycle and the α-glycerophosphate shunt against the background of an increase of the lymphocyte concentration in the complete blood count up to 65% (the level of calm activation reaction) against 45% in the reference test (the level of stress). It indicates not only an anti-stressor effect of VLF MF, but also the control provided by the latter over concentration of ferments-bio-regulators which govern the mechanisms of cell metabolism [13].

The said specific features of the influence made by VLF MF were also confirmed later: week 5 and week 9

of cancerogenesis demonstrated the maintenance of the activity of SDH which is of particular value for synthesis of energy-rich compounds. The regulation of SDH in the processes, which require an economical ATP synthesis, such as proliferation, in the opinion supported by Davidson J. [12], is performed by changing the ATP concentration. Under peak load conditions in an organism, demanding urgent production of ATP, it is just SDH that plays the major role in the organism for this purpose. The mechanism of activation of SDH is related to an elevation of the restorability of the components of the mitochondrial respiratory chain under the “working” hypoxia, as well as to an increase of succinic acid supply with burning lipids and proteins [14-19].

The stable distinguishing feature of the activity of SDH in lymphocytes in peripheral blood in rats exposed to VLF MF under cancerogenesis, that has been detected by us, makes possible to assess one more physiological aspect of the regulation of the activity of the ferment. It is linked with the

necessity to avoid an excessively intensive oxidation of succinic acid that may involve not only depletion of substrates, but also a disagreement in the respiration processes and phosphorylation. But at the same time, in spite of the completed VLF MF exposures, the fact of a reduction in the activity of α -GDPH was reported, that was scarcely exhibited in week 5 and clearly detected in week 9 of the chemical cancerogenesis (see Figure 1).

For an interpretation of the possible mechanism, it is required to take into account the linkage between α -GDPH and some specific functions of lymphocytes, namely, their immune, trophic functions etc. It has been established that the condition of differentiation of lymphocytes is determined by the respective level of activity of dehydrogenases [13-17]. In this case, it should be noted that the ferment activity in immature lymphocytes is higher than that in mature ones, and an increase in the relation between α -GDPH and SDH may be used as an indicator of the "rejuvenation" of the cell population. Following this interpretation way, we can state that a reduction in the activity of α -GDPH in relation to SDH under VLF MF exposure may indicate that there is an increase in the pool of mature lymphocytes. The research literature offers a knowledge of high informative value of the morphometric markers of immune competent cells in blood in oncology patients suffering from blood cell production disorders, and one of the markers is considered to be the absence of the small (mature) lymphocytes and an increase in the averaged area of the lymphocytes at the expense of expanding the volume of the cytoplasm. So, it is logical to suppose that in case of cancerogenesis, under VLF MF

exposure, there certain conditions of the internal environment are being formed, which provide for preservation and an increase in the number of the mature differentiated immune competent cells responsible for anti-tumor resistance.

In order to validate our hypothesis, we have studied the fermentative activity of lymphocytes in local-type mammary gland cancer patients under their autochemotherapy with the use of optical magnetic treatment (OMT) of blood. It has been established that the initial activity of SDH according to the averaged amount of formazan granules (Mav) (before the treatment) has been recorded at a level of 16,5 – 19,8 in conventional units. As this takes place, the pool of the cells showing a high concentration of ferment-containing granules (Ja) has reached a level of $224 \pm 2,4$ in conventional units, that has been reflected in the relationship between the SDH-activated lymphocytes and the null-subpopulation cells (Jo). Taking into account that we were dealing with not a generalized, but a local form of the cancer, we might suggest that the mechanisms of the energy production in the circumstances are active enough to meet the demands of the organism which is competing against a progressing tumor.

Upon the completion of chemotherapy (therapy course 1), the activity of SDH was reported to be lowered to 9,8 – 13,3 in conventional units, with the Ja-level reduction to $190 \pm 17,5$ in conventional units and the Ja/Jo-relation decrease to 1,85. This condition has characterized the suppression of the respiratory processes and oxidative phosphorylation of the blood lymphocytes. This bears witness to the stressogenic effects of cytostatic

agents on the energy metabolism as one of the most important members in the bio-adaptive integral responses by an organism.

The group of patients who received a combination of chemotherapy and OMT for peripheral blood has demonstrated the condition of fermentative activity of lymphocytes that has been characterized by the actual keeping of the initial values of SDH, and the count of the exhausted lymphocytes has been recorded to be very low. An indication of a higher level of involvement of ferments in energetics of lymphocytes was an increase in relation Ja/Jo by 2.3 times. Upon completion of chemotherapy course 2, the dynamics of the SDH activity in the reference group was reported as negative. For the main group exposed to OMT, against the background of the maintenance of the activity of SDH, there has been reported a response of the α -GDPH activity that has been synchronized by criteria Ja and Ja/Jo with the Krebs cycle process level. Glycolysis boosting was not prolonged; observed were coming into action of the regulatory mechanisms, correction and protection from acidosis.

This is the supporting evidence for the opinion by M.N.Kondrashova and I.E.Maevski that "the mitochondrial approach" is very productive in an organism and that moreover it demonstrates a high prognostic value when assessing treatment efficacy.

We may conclude that the behavior of the cell systems illustrated by an example for the lymphocyte population in the peripheral blood is subjected to a regularity of the formation of an adaptive response, with developing the trigger mechanisms, which may be induced by some factors of electromagnetic nature: VLF MF and OMT. This mechanism implements

the systems of metabolic re-setting on the cell membranes of lymphocytes, weakening inhibition influence of tumor growth on fermentative activity.

By this means an assessment of metabolic correction of lymphocytes as one of the principal members of the immunological protection under tumor diseases and other critical pathological conditions can bear witness to a degree of involvement of physiological resources of an organism in the processes of elevation of unspecific resistance. The simple assessment criteria for energetics in an organism provides us with the "online" information about efficacy of the correction of pathological disorders and the real forecast of stability of treatment in oncology, cardiology and other most important fields in medicine.

Statement on ethical issues

Research involving people and/or animals is in full compliance with current national and international ethical standards.

Conflict of interest

None declared.

Author contributions

The author read the ICMJE criteria for authorship and approved the final manuscript.

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