Aspects Of Cellular Energy Metabolism Disorders In Somatic Diseases In Pediatrics

Arzibekov Abdikadir Gulyamovich

Andijan State Medical Institute, Head of the Department of Pediatrics, Faculty of Medicine, Candidate of Medical Sciences, Docent.

ABSTRACT

Modern views on energy metabolism in a living cell are presented, information is presented on the mechanisms of its implementation in normal conditions and in pathology. Methods for diagnosing disorders of intracellular energy are covered in detail, including assessment of the activity of mitochondrial enzymes in blood lymphocytes, the level of total and bound carnitine using photoelectrocolorimetry and liquid tandem chromatography-mass spectrometry methods. The main clinical manifestations of mitochondrial disorders are described: pathological manifestations of the muscular and central nervous systems, heart, other somatic organs, multisystemic lesions.

Keywords: mitochondrial disorders, children, connective tissue dysplasia, L-carnitine, mitochondrial diseases, energy-tropic therapy.

Introduction

Energy exchange is a complex complex of processes that ensures all aspects of the life of living matter. It includes chemical and physicochemical reactions both in the body as a whole and at the level of an individual cell. Recently, modern medicine has been paying increasing attention to the processes underlying cellular energy supply that occur in mitochondria. The main function of these organelles is to produce energy from metabolic products entering the cytoplasm. It is in them that cellular respiration occurs, substances obtained as a result of anaerobic fermentation are oxidized and a large amount of energy is released, accumulated mainly in ATP. Disturbances in the processes of normal metabolism in mitochondria are called mitochondrial insufficiency.

Materials And Methods

Metabolic disorders caused by mitochondrial dysfunction, damaging tissue respiration, were first described in the middle of the 20th century. Currently, more than 200 diseases are known that are caused by genetic, structural, and biochemical defects in organelles, which are based on mitochondrial insufficiency as an etiological or pathogenetic factor. These include diabetes mellitus, rickets, chronic fatigue syndrome, glycogenosis, liver failure, proximal tubulopathy, migraine, pancytopenia, hereditary connective tissue disorders and many others. Most often, clinical manifestations in various combinations are observed from the central and peripheral nervous systems, skeletal and cardiac muscle tissue, sensory organs, endocrine and exocrine glands. These may be low tolerance to physical activity, fatigue, weakness, muscle hypotonia, hypotrophy, myopathic syndrome, mental retardation, convulsions, hypertrophic or dilated cardiomyopathy, disorders of cardiac conduction, vision and hearing, metabolism [1].

Results And Discussion

Along with proteins and carbohydrates, the main sources of energy in the cell are fats. One

of the most important stages of obtaining energy from them is the oxidation of fatty acids in mitochondria, followed by the synthesis of ATP. The level of ATP synthesis depends on the entry of fatty acids into these organelles. A key participant in this process is considered to be L-carnitine, which is found in tissues in the form of the L-stereoisomer. L-carnitine is a low molecular weight compound derived from aminobutyric acid. It transports long-chain fatty acids in the form of esters (acylcarnitines) from the cytoplasm through the outer and inner mitochondrial membranes into the matrix. There, in the matrix, their β-oxidation occurs with the formation of acetyl-CoA, which serves as a substrate for the Krebs cycle and the subsequent synthesis of ATP, choline and its esters, from which acetylcholine is formed [2, 3]. The participation of L-carnitine in the synthesis of non-mediator intracellular acetylcholine by T- and B-lymphocytes has been proven. The latter interacts with the corresponding receptors on splenic macrophages, inhibiting the activity of the inflammatory mediator tumor necrosis factor-alpha, responsible for the development of systemic inflammation [4]. Acetylcholine, being a mediator of both the sympathetic and parasympathetic parts of the autonomic nervous system, ensures the body's adaptation to the influence of environmental factors [1]. The beneficial effect of L-carnitine on the vascular endothelium has been established. Its ability to restore endothelial function and prevent vascular remodeling caused by a decrease in nitric oxide production has been revealed [2].

In the human body, only 10-20% of the required amount of carnitine is synthesized in the liver and kidneys from a precursor with the participation of the amino acids lysine, methionine and a number of enzymes in the presence of vitamins C, B, and iron ions. The resulting carnitine is transported to skeletal muscles and myocardium, its storage tissues, where fat metabolism actively occurs. 80-90% of the required amount of carnitine should come from outside. Currently, an adult's menu provides only a third of his carnitine needs, mainly through meat, dairy and fish products (hence its name from "karnis" - "meat").

Currently, secondary deficiency of this biologically active substance is common in the population. The reasons lie in violations of its endogenous synthesis, absorption from food, metabolism in the body, insufficient intake from food, and in increased excretion through the kidneys or digestive tract. Normally, carnitine is almost completely reabsorbed in the kidneys. Its removal from the body increases during stressful situations, infectious diseases, dysfunction of the renal tubules, pathology of the liver and intestines [2].

Disturbances in the processes of cellular energy exchange are indirectly or directly indicated by metabolic acidosis, an increase in the blood levels of lactate and pyruvate on an empty stomach and after a glucose load, a change in the lactate/pyruvate ratio, activation of lipid peroxidation, an increase in the excretion of a number of organic acids, and a decrease in the content of total carnitine. Total blood carnitine is the sum of free (70–80%) and bound species (20–30%). Normally, the level of free carnitine in the blood is 20–60 μmol/l. Its indicators reflect the release of this substance from the endogenous pool. Bound carnitine is represented by acylcarnitines, mainly acetylcarnitine C2 (85%). It is informative to study the ratio of bound and free carnitine - the carnitine coefficient; it usually does not exceed 0.6. Its increase while maintaining the level of total carnitine within the reference values indicates a relative deficiency of free carnitine [2].

The above data on various deviations are not specific, they are variable and can occur both in mitochondrial deficiency and in other diseases. In general, 15–20% of children have moderate disorders of cellular energy. They may not manifest themselves as independent diseases, but they affect the course of other diseases [2].

In athletes experiencing increased physical activity, taking L-carnitine contributed to a decrease in the size of the left ventricle of the heart and restoration of the initially impaired systolic function (ejection fraction) [3]. The effectiveness of energotropic therapy in

children with mitral valve prolapse has been proven.

L-carnitine preparations are often prescribed for autonomic disorders in children and adolescents. When one of the sections of the autonomic nervous system dominates, the body's energy needs noticeably increase, which leads to the development of tissue hypoxia, intracellular acidosis and energy deficiency [2]. T.N. Nakostenko et al. included in their study 50 frequently ill children aged 5–10 years with different types of vegetative-vascular dystonia [3]. The treatment used a combination of 20% Elcar and Pantogam in standard doses for 1 month. As a result of therapy, improvements in cognitive and emotional functions, parameters of autonomic homeostasis, and indicators of mitochondrial enzyme activity were noted. The authors conclude that, in general, this complex of drugs is effective. The most pronounced positive trends were obtained in children with normotonic autonomic reactivity [5]. In the asympathicotonic variant, when less pronounced positive changes were observed as a result of treatment, the body's reserve capabilities are assessed as lower and largely exhausted [3].

Conclusion

Thus, an analysis of literature data shows that cellular energy deficiency is a fairly common condition in children. It accompanies many somatic diseases, to a certain extent slowing down recovery and creating an unfavorable background, and occurs in mitochondrial disorders. The combination of damage to the central nervous system, heart and muscles is an indication for examination for mitochondrial diseases. Energy-deficient diathesis is a term that can increasingly be found in modern medical literature [2].

References

1. Dumova S.V., Chugunova O.V. Correction of intracellular energy metabolism in premature newborns with intrauterine growth retardation. Pediatrics 2016; 95(1): 17–23.
2. Sukhorukov V.S. Essays on mitochondrial pathology. M: ID MEDPRACTIKA-M 2011; 288.
3. Neudakhin E.V. The feasibility of using carnitine preparations in the treatment of chronic eating disorders in children. Pediatrician Practice 2015; 2:48–52.
4. Fujii T., Takada-Takatori Y., Kawashima K. Basic and clinical aspects of non-neuronal acetylcholine: expression of an in-dependent, non-neuronal cholinergic system in lymphocytes and its clinical significance immunotherapy. J Pharmacol Sci 2018; 106:186–192.
5. Neudakhin E.V., Talitskaya O.E. On the advisability of using carnitine preparations in the treatment of vegetative dystonia syndrome in children. Pediatrician Practice 2017; 1:38–45.