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IMPACT OF A NOVEL AMINO ACID-BASED BLOOD SUBSTITUTE ON CORE METABOLIC HOMEOSTASIS PARAMETERS DURING PROTEIN-ENERGY MALNUTRITION

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Abstract. Protein-energy deficiency remains a significant medical problem and is often associated with disturbances of metabolic homeostasis in various athological conditions. The aim of this study was to evaluate the effects of a novel amino acid–based blood substitute, Aminoyantar, on key indicators of metabolic homeostasis under experimental protein-energy deficiency. The experiment was conducted on 120 laboratory rats. It was found that protein-energy deficiency led to noticeable changes in erythroid parameters, as well as disturbances in protein metabolism, energy metabolism, and the antioxidant defense system.

Administration of Aminoyantar contributed to the improvement of these parameters. In our observations, its effect appeared more pronounced compared to Infesol-40.

Overall, the findings suggest that Aminoyantar may be considered an effective agent for correcting metabolic homeostasis under conditions of protein-energy deficiency.

Keywords: protein-energy deficiency, metabolic homeostasis, Aminoyantar, Infesol-40, antioxidant system, HIF-1α.

Abstract: Protein-energy deficiency is one of the important medical problems accompanied by metabolic homeostasis disorders in various pathological conditions. The purpose of this study was to evaluate the effect of a new amino acid-based blood substitute, Aminoyantar, on metabolic homeostasis parameters under experimental protein-energy deficiency conditions. The study was conducted on 120 laboratory rats. The obtained results showed that protein-energy deficiency leads to significant changes in erythroid parameters, as well as in protein and energy metabolism, and the antioxidant defense system. The use of Aminoyantar led to the improvement of these parameters and demonstrated higher efficacy compared to Infesol-40. The obtained results indicate that Aminoyantar is an effective agent in the correction of metabolic homeostasis under conditions of protein-energy deficiency.

Keywords: protein-energy deficiency, metabolic homeostasis, Aminoyantar, Infesol-40, HIF-1α, lipid peroxidation, antioxidant system, liver, kidney.

Introduction: Currently, the problem of protein-energy deficiency occurring in various pathological conditions is globally recognized as one of the urgent medical issues. This condition plays a significant role in the progression of many diseases and, in some cases, is associated with high mortality rates. In this regard, studying how the main components of metabolic homeostasis are disrupted during the development of protein-energy deficiency remains a priority in modern medicine [1,3,7].

It is known that protein-energy deficiency triggers the development of several pathological processes in the body, and this condition is accompanied by the disruption of metabolic homeostasis. As a result, cellular energy and plastic metabolism processes are impaired, free radical oxidation of lipids intensifies, and the activity of the antioxidant defense system decreases. Such changes negatively affect the overall functional state of the body and can lead to internal organ dysfunction.

Therefore, the search for and development of effective therapeutic agents aimed at eliminating the imbalance in the homeostasis system under conditions of protein-energy deficiency are of great scientific and practical importance [4,8,10].

Today, many scientific studies are being conducted worldwide to identify effective methods for correcting metabolic homeostasis disorders under conditions of protein-energy deficiency. In particular, investigating the effect of new blood substitutes with antioxidant properties on protein and energy metabolism is a highly relevant direction. At the same time, special attention is paid to evaluating the activity of hypoxia-inducible factor (HIF-1α), lipid peroxidation processes, and the state of the antioxidant system. In addition, identifying the morphological changes that occur in the liver and kidneys during protein-energy deficiency holds significant scientific importance [2,6,9].

Protein-energy deficiency manifests as a disruption in the functioning of body cells and internal organs. This condition can lead to a severe course of underlying diseases, a decline in the quality of life, cognitive impairment, and an increased risk of severe complications and mortality. Thus, it is crucial to apply treatment measures aimed at rapidly and effectively restoring the protein deficiency that has occurred in the body [5,11].

Studies conducted by local scientists have noted the effectiveness of preparations based on sodium succinate. Additionally, biologically active substances with detoxifying, antioxidant, antiviral, and immunomodulatory properties have been found to exert a positive effect on restoring the impaired functions of cells and organs [13,14].

Nevertheless, the pathogenetic mechanisms of protein-energy deficiency have not been fully elucidated. This requires a deeper investigation into the disorders within the main components of metabolic homeostasis and the development of new, effective methods for correcting this condition [10,12]. In this regard, studying the effect of a new amino acid blood substitute, Aminoyantar, on metabolic homeostasis parameters under protein-energy deficiency conditions is an urgent scientific task [15].

Aim of the study: To investigate the effect of the amino acid blood substitute Aminoyantar on protein and energy metabolism, the hypoxia-inducible factor HIF-1α, lipid peroxidation, and antioxidant system parameters in protein-energy deficiency.

Materials and Methods of the Research: The study was conducted on 120 white, outbred rats weighing 180–220 g, housed under vivarium conditions at the Republican Specialized Scientific and Practical Medical Center of Hematology. The experimental animals were divided into 4 groups. The first group consisted of intact animals on a complete feeding diet. In the second group, a protein-energy deficiency model was induced by feeding a protein-free diet for 10 days. In the third group, following the induction of the model, the amino acid preparation Infesol-40 was administered at a dose of 10 mg/kg for 10 days. In the fourth group, after the model was established, the new local amino acid blood substitute Aminoyantar was administered intraperitoneally at a dose of 10 ml/kg for 10 days. The study evaluated general blood count parameters, protein status, enzyme activity, nitrogen, carbohydrate, lipid, and energy metabolism parameters, HIF-1α levels, lipid peroxidation, and antioxidant system parameters, as well as the morphological state of the

liver and kidney tissues. Statistical analysis was performed using Microsoft Office Excel-2018 software.

Results and Discussion: The research results demonstrated that significant changes occurred in the main components of metabolic homeostasis in the rats with the experimental protein-energy deficiency model. First and foremost, pronounced changes were observed in peripheral blood parameters. Under protein-energy deficiency conditions, a 1.24-fold decrease in hemoglobin levels (102.2±1.3 g/l), a 1.7-fold decrease in the erythrocyte count (2.28±0.08×10^{12}/l), and a 1.6-fold decrease in the reticulocyte count (4.12±0.36 ‰) were detected, indicating the development of anemia in the experimental animals. At the same time, while platelet, leukocyte, and ESR parameters remained within normal limits, certain shifts in their levels were recorded compared to the intact group. These results align with data obtained by other researchers regarding the disruption of hematological parameters in protein-energy deficiency [3,7].

Significant impairments in protein status were also found under protein-energy deficiency conditions. Specifically, the total protein level decreased by 22.8% to 56.1±0.7 g/l, whereas in the intact group, this indicator was 72.63±0.67 g/l. The albumin level decreased by 21% to 22.7±0.3 g/l. Similarly, the globulin level decreased by 23.7% to 33.42±0.42 g/l. Among the globulin fractions, the most substantial decline was observed in the β-fraction and α2-fraction. The β-fraction decreased by 43% to 8.5±0.1 g/l, while the α2-fraction decreased by 41% to 4.6±0.06 g/l. These changes indicate that protein metabolism processes in the body are significantly disrupted under conditions of protein-energy deficiency, which is corroborated by the findings of other authors [1,4].

Energy metabolism parameters also underwent significant changes. In the experimental animals, Na^+/K^+-ATPase activity decreased 1.5-fold to 10.6±0.1 µmol Pi/s/ml, compared to 16.2±0.15 µmol Pi/s/ml in the intact group. Mg^{2+}-ATPase activity also decreased 1.4-fold to 19.6±0.3 µmol Pi/s/ml. Additionally, the concentration of potassium ions in the plasma decreased 1.3-fold to 4.11±0.04 mM, while the concentration of sodium ions dropped to 137.9±0.9 mM. These changes reflect the disruption of intercellular ion transport and energy metabolism processes. Similar metabolic shifts have been noted in other studies as well [8,10].

Under conditions of protein-energy deficiency, the metabolic imbalance was accompanied by liver and kidney dysfunction. This was manifested by an increase in enzyme activity. Specifically, ALT activity increased 1.42-fold to 25.7±0.66 U/l, and AST activity increased 1.54-fold, reaching 17.9±0.5 U/l. Creatine phosphokinase (CPK) activity also increased nearly 1.4-fold to 201.5±8.7 U/l. Lactate dehydrogenase (LDH) activity rose 1.35-fold to 444.6±10.6 U/l. These findings regarding impaired liver and kidney functions are consistent with the data of other authors [2,9].

Nitrogen metabolism parameters were also notably altered. The urea level increased 2.2-fold to 10.75±0.55 mmol/l. The creatinine level increased 1.66-fold, reaching 115.3±4.97 mmol/l. These changes point to renal dysfunction and are confirmed by the results of other studies [5,11].

Regarding carbohydrate metabolism, the glucose level sharply declined to 2.09±0.11 mmol/l. In lipid metabolism, the triglyceride level decreased 4.9-fold to 0.22±0.04 mmol/l, and the total cholesterol level decreased 1.9-fold. Such metabolic shifts are attributed to the disruption of energy metabolism under protein-energy deficiency conditions [6,12].

The development of a hypoxic state was also observed under protein-energy deficiency conditions. This was evidenced by a 1.6-fold increase in the level of the hypoxia-inducible factor HIF-1α, reaching 0.11±0.004 ng/ml. This indicator suggests that hypoxic processes in the body had intensified [8].

Lipid peroxidation processes were also significantly activated. The level of malondialdehyde (MDA) in the plasma increased 1.6-fold, and MDA in erythrocytes increased 1.7-fold. Likewise, the levels of diene ketones and diene conjugates increased 1.7-fold. Simultaneously, the parameters of the antioxidant system significantly declined. Total antioxidant status decreased 1.84-fold. It was noted that the activity of erythrocyte catalase, glutathione reductase, glutathione peroxidase, and superoxide dismutase enzymes also sharply decreased. This indicates that the balance between the prooxidant and antioxidant systems in the body was disrupted [10,12].

Morphological examinations revealed dystrophic and dysregenerative changes in liver and kidney tissues. Irreversible morphological alterations were observed in intracellular structures, which is explained by the consequent disruption of metabolic homeostasis [9].

Following the administration of Infesol-40 and Aminoyantar preparations, positive dynamics across multiple parameters were observed in the experimental animals. However, after the administration of Aminoyantar, hemoglobin, erythrocyte, and reticulocyte levels recovered much closer to the values of the intact group. For instance, after using Infesol-40, the hemoglobin level was 7% lower compared to the intact group, whereas after using Aminoyantar, this difference was merely 2.1%.

A similar positive dynamic was noted in protein status parameters. The levels of total protein, albumin, and globulin fractions were restored to a significantly higher degree following Aminoyantar administration compared to Infesol-40. Energy metabolism parameters also saw substantial improvement under the influence of Aminoyantar. ATP concentration, Na^+/K^+-ATPase and Mg^{2+}-ATPase enzyme activities, as well as plasma ion levels, were restored to a greater extent than with Infesol-40.

Furthermore, positive shifts were observed in parameters related to nitrogen, carbohydrate, and lipid metabolism. Urea and creatinine levels decreased, while glucose, triglycerides, and total cholesterol levels increased. The level of HIF-1α also notably decreased post-treatment. A comparative analysis of lipid peroxidation and antioxidant system parameters further demonstrated the high efficacy of Aminoyantar. The levels of MDA, diene ketones, and diene conjugates significantly decreased, and the activity of antioxidant enzymes was restored.

Morphological studies also corroborated the high efficacy of Aminoyantar. Following the application of the preparation, the restoration of metabolic processes and the improvement of cellular structures in the liver and kidney tissues were observed. These results indicate that Aminoyantar possesses high efficacy in restoring metabolic homeostasis [13–15].

Conclusion: The conducted studies have shown that under experimental protein-energy deficiency conditions, significant disruptions occur within the main components of metabolic homeostasis. This condition manifests as a reduction in the formation of erythroid elements, a decrease in hemoglobin levels, a decline in total protein and its fractions, the disruption of energy metabolism processes, and the impairment of ion transport across cell membranes. Concurrently, an increase in the level of HIF-1α, the activation of lipid peroxidation processes, and a decrease in antioxidant system activity are observed.

It was established that functional and morphological changes develop in the liver and kidneys under experimental protein-energy deficiency. Specifically, this included elevated activity of liver enzymes (ALT, AST), creatine phosphokinase, and lactate dehydrogenase; increased nitrogen metabolism parameters; and dystrophic and dysregenerative changes in liver and kidney tissues.

Through comparative analysis, the positive impact of Infesol-40 and the new local amino acid blood substitute preparation—Aminoyantar—on correcting metabolic homeostasis disorders was identified. However, upon the application of Aminoyantar, the restoration of peripheral blood

parameters, protein metabolism, energy metabolism, lipid peroxidation, and antioxidant system metrics was notably more pronounced than with Infesol-40.

The high efficacy of Aminoyantar is explained by its compositional characteristics. The amino acids within the preparation assist in restoring protein metabolism, while sodium succinate activates energy metabolism and exerts an antihypoxic effect. The combined action of mannitol and sorbitol reduces the free radical oxidation of lipids and enhances the activity of the antioxidant system. Consequently, cellular energy processes are activated, metabolic homeostasis is restored, and the functional state of internal organs improves.

Thus, the obtained results demonstrate that Aminoyantar is highly effective in correcting metabolic homeostasis disorders under experimental protein-energy deficiency conditions. This preparation facilitates the recovery of metabolic processes in liver and kidney tissues, thereby offering the potential to improve treatment efficacy in these pathological conditions.

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