

Creation of Infusion Solutions with Pathogenetically Deterministic Composition on the Basis of Regulatory Actions of Free Amino Acids and their Derivatives

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Summary

As a practical application of the regulatory action of amino acids and their derivatives for the elimination of amino acid imbalance and metabolic therapy for specific indications proposes a methodology for the development of new multi-local amino acid mixtures according to the pathogenesis deterministic changes in their physiological concentrations.

Keywords: Free amino acids; Regulatory effects; Infusion solutions

Development and continuous improvement of high-performance and highly sensitive chromatographic methods allowed amino acid analysis to determine the physiological concentrations (10^{-9} - 10^{-12} M) of the compounds of this class and their derivatives in biological material [1,2].

Numerous results of determination of amino acids and their derivatives in human body fluids and tissues, resulting in the 70-ies [3] allowed to systematize the accumulated data and identify areas for exploitation of their metabolic effects, primarily - in laboratory diagnostics and application in clinical practice as drugs [4].

The most significant number of studies devoted to the search marker amino acids or their derivatives for the diagnosis of various diseases. Since the free amino acids are represented by a wide range of related chemical structure and metabolic transformations of compounds that form in the body fluids and tissues amino fund proved that quantification of their pool contributes to the diagnosis of various diseases, including hepatobiliary pathology, cardio-vascular and immune systems, oncological causes, cerebrovascular pathology, alcoholism and diabetes [4-8].

It turned out that the vast majority of the diagnostic value of the group has shifts in the level of functional and metabolic-related amino acids and their derivatives, and no specific changes in the concentrations of individual compounds of this class. In this highly informative enough had the nature of the amino acid profiles of the body fluids and tissues of animals and humans when compared with the use of multivariate analysis and mathematical modeling [9,10].

At the same time, convincingly demonstrated that the removal or correction of the intermediate metabolic changes can be achieved using individual amino acids and their derivatives, or a combination thereof as universal natural bioregulators - compounds that affect directly on the mechanisms of cellular metabolism in physiological (endogenous) concentrations [5-9].

To date, there is evidence of the importance of not only amino acids as building blocks for protein synthesis, but regulators of gene expression at the level of mRNA translation by mTOR-dependent mechanism, signaling molecules and biological response modifiers, as well as precursors of a wide range of bio-regulators, which play a key role in the integration major metabolic fluxes [11-13].

Based on the positions of metabolomics, the amino acid pool of biological fluids and tissues fund free amino acids evaluated as a single information unit, which is a kind of "chemical projection" of the genome, proteome realized through. This approach not only develops ideas about the pool of amino acids as a dynamical system generated receipt of them from outside, and also due to endogenous synthesis, transport, degradation and excretion, but also allows to identify "key points" intermediate metabolic equilibrium shift that may reflect ratios at the individual levels of endogenous amino acids and related species (metabolic related) compounds [8,9].

Under current conditions in the complex treatment of patients with one of the leading ranks of infusion-transfusion therapy, which is based on the use of blood products. However, so far not developed effective transfusion media capable of long-circulate in the blood, improve hemodynamics, microcirculation and simultaneously have directed metabolic (regulatory) effect on key metabolic reactions and functions. Thus, the use of plasma expanders for infusion therapy contributes to the implementation of one or more tasks, leaving the other, no less important, in the background, which complicates the most adequate treatment [14].

Recently, experimental and clinical transfusion growing preference development and application of multicomponent solutions polyfunctional blood substitutes. Significant place in this direction occupy solutions artificial mixtures of highly purified amino acid substances. When this amino acid-based drugs (Polyamine (Russia), Aminosteril KE 10% (Germany), Vamin (Sweden), Friamin (USA) and many others are designed primarily based on the daily protein

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requirements for maintain a positive nitrogen balance and are used primarily with the aim of substitution [14-16].

Furthermore, on the basis of organ specificity and features metabolism to implement biochemically reasoned action of individual amino acids are developed and implemented specialized compounding their artificial mixtures combining conditions of parenteral nutrition and pathogenic correction of liver pathology ("hepatoaminosols"), kidney ("nephroamins") or application in pediatric practice ("aminoped").

Such amino acid solutions contain significantly more (branched) or less (aromatic, sulfur) number of individual amino acids or substances mainly include (nephrotoxicity) essential amino acids. In assessing the effectiveness of this group aminosols use the results of clinical laboratory research and the criteria for their specific pharmacological activity.

Aminosols these listed properties for parenteral nutrition in practice determine the necessity of their combined (combined or sequential) application with drugs other groups, which complicates the implementation of therapeutic interventions and can cause amino acid imbalance [4-9,14].

The accumulated experience of clinical use of foreign and domestic drugs individual highly purified amino acids ("Taurine", "Leucine", "Tryptophan") or minicompositions ("Tavamin", "Tryptamine", "Neyramin") indicate the possibility of the application of multicomponent solutions with a concentration of each amino acid compound calculated in accordance with its metabolic profile in human blood at a particular disease [9].

Our proposed methodology for developing new formulations multicomponent infusion solutions based on amino acids and related compounds for the correction occurring in various diseases of the metabolic imbalance, based on the application of research results regularities of formation of amino acid fund in biological fluids and tissues in various pathological conditions [17].

The composition and quantity of highly purified amino acids in these infusion solutions should be determined primarily by their physiological (endogenous, regulatory) concentrations, which distinguishes them from the traditionally used amino acid solutions for parenteral nutrition, where the content of their components is calculated based on the daily needs of the human body in them without due consideration regulatory actions administered compounds.

Proposed to develop multi-infusions of amino acids due to the high degree of poly-functionality, biocompatibility, lack of antigenic properties and stable hemodynamic efficacy should have a comprehensive action in the direction of "metabolic comfort" and, combining not only different functions hemocorrectors be absolutely safe, not cause allergic reactions, prevents the development of complications caused by damage of various origins [18].

Our development methodology is based on:

1. Study of physiological concentrations of free amino acids, their derivatives, precursors and metabolites, as well as biochemical marker parameters in healthy donors and patients with various pathologies;
2. Creating a unified database for the studied parameters, the construction of empirical mathematical model consisting of pathogenic markers specific pathology and amino acid profiles;
3. Specialized development of new formulations of the compositions of infusion solutions of amino acids and their derivatives.

Thus, the development and establishment of the Republic of Belarus in the new multi-domestic amino acid mixtures according to the pathogenesis deterministic changes in their physiological concentrations to eliminate amino acid imbalance and metabolic therapy for specific indications is one of the elements of exploitation of regulatory action of this class of compounds.

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