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FEATURES OF AMINO ACID METABOLISM IN CHILDREN WITH ACUTE RESPIRATORY VIRAL INFECTIONS

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Abstract. *Introduction.* Children with ARVI may have different signs during a routine medical examination, including incidental detection of abnormal Liver function tests, Amino acid metabolism disorders, Jaundice or Hepatomegaly due to Hepatobiliary system dysfunction.

The aim was to investigate and analyze the state of Amino acid metabolism in Acute Respiratory Viral infections in children.

Materials and methods. The study group consisted of 60 children diagnosed with Acute Respiratory Viral infections (ARVI) and identified Adenovirus infection who were receiving inpatient treatment at the OKIL KNP «Center for Lung Diseases» of the Zakarpattya Regional Council. The study included non-essential Amino acids (Alanine and Glycine), essential Amino acids (Tryptophan, Methionine, Phenylalanine) and the conditionally essential Amino acid - Tyrosine.

Results. We conducted a study of the Amino acid composition of blood serum in children in accordance with the tasks of the investigation. The study included non-essential Amino acids (Alanine and Glycine), essential (Tryptophan, Methionine, Phenylalanine) and conditionally essential Amino acid – Tyrosine. The levels of all studied Amino acids varied within the reference values but had significant differences compared to the data of the control group, in particular: Alanine (294.65±64.68 versus 430.27±55.81 μmol/l in comparation to the control group data, p1<0.001); Glycine (228.62±47.65 versus 315.38±43.28 μmol/l, p1<0.001); Tryptophan (39.74±10.53 versus 57.48±7.11 μmol/l, p1<0.001); Methionine (19.04±3.33 vs. 26.25±4.19 μmol/l, p1<0.001); Phenylalanine (46.47±8.80 vs. 56.40±6.93 μmol/l, p1<0.001); Tyrosine (47.03±5.86 vs. 60.35±5.18 μmol/l, p1<0.001).

Conclusions. The conducted studies revealed Amino acid levels within the reference values in children with ARVI, but with significant decreases in values compared to the control group.

Key words: Amino acids, metabolism, ARVI, children.

Особливості обміну амінокислот у дітей із гострими респіраторними вірусними інфекціями
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Резюме. *Вступ.* У дітей при ГРВІ можуть спостерігатися різноманітні ознаки під час планового медогляду, зокрема випадкове виявлення аномальних показників функції печінки, порушення обміну амінокислот, жовтяниця або гепатомегалія внаслідок дисфункції гепатобіліарної системи.

Мета дослідження. Дослідити та проаналізувати стан амінокислотного обміну при гострих респіраторних вірусних інфекціях у дітей.

Матеріали та методи. Досліджувана група складала 60 дітей із діагнозом ГРВІ та ідентифікованою аденовірусною інфекцією, які перебували на стаціонарному лікуванні в ОКІЛ КНП «Центр легеневих хвороб» Закарпатської обласної ради. Досліджувалися замінні амінокислоти (аланін і гліцин), незамінні (триптофан, метіонін, фенілаланін) та умовно незамінна амінокислота – тирозин.

Результати досліджень. Нами було проведено дослідження амінокислотного складу сироватки крові у дітей. Досліджувалися замінні амінокислоти (аланін та гліцин), незамінні (триптофан, метіонін, фенілаланін) та умовно незамінна амінокислота – тирозин. Рівні всіх досліджуваних амінокислот коливалися в межах референтних величин і мали достовірні відмінності порівняно з даними контрольної групи, зокрема: аланін (294,65±64,68 проти 430,27±55,81 мкмоль/л у контрольній групі, p_1<0,001); гліцин (228,62±47,65 проти 315,38±43,28 мкмоль/л, p_1 < 0,001); триптофан (39,74±10,53 проти 57,48±7,11 мкмоль/л, p1<0,001); метіонін (19,04±3,33 проти 26,25±4,19 мкмоль/л, p_1<0,001); фенілаланін (46,47±8,80 проти 56,40±6,93 мкмоль/л, p_1<0,001); тирозин (47,03±5,86 проти 60,35±5,18 мкмоль/л, p_1<0,001).

Висновки. Проведені дослідження виявили рівні амінокислот у межах референтних величин у дітей із ГРВІ, але з достовірними зниженнями значень порівняно з даними контрольної групи.

Ключові слова: амінокислоти, метаболізм, ГРВІ, діти.

Introduction

Children with acute respiratory viral infections may presented different symptoms, including incidental findings of abnormal Liver function tests during routine physical examination, Jaundice, or Hepatomegaly due to Hepatobiliary dysfunction. In a study of 147 children with Acute Acalculous Cholecystitis (gallbladder inflammation in the absence of gallstones), the most common clinical manifestations were elevated CRP (84%), Hepatomegaly (80%), and Anorexia (78%). Acute Acalculous Cholecystitis in children has been associated with a variety of comorbidities, including infectious (70%), systemic (13%), and malignancies (11%) [1]. Metabolic interactions between the patient's antioxidant system and pathogens during infection are a natural mechanism of protection against the pathological consequences of infection. Today, there are many studies devoted to the study of metabolic adaptation during infection, but this process should be considered in conjunction with the characteristics of the pathogen and the resources of the patient's organism. The term «immunometabolism» and the study of its components are extremely promising and promising for the analysis of the organism's protective processes, as well as for the development of strategies for the prevention of pathological influences and the correction of their harmful consequences [2,3].

The aim was to investigate and analyze of the Amino acid metabolism state in Acute Respiratory Viral infections in children.

Materials and methods

The study group consisted of 60 children diagnosed with Acute Respiratory Viral infections (ARVI) and identified Adenovirus infection who were receiving inpatient treatment at the OKIL KNP «Center for Lung Diseases» of the Zakarpattya Regional Council. The study included non-essential Amino acids (Alanine and Glycine), essential Amino acids (Tryptophan, Methionine, Phenylalanine) and the conditionally essential Amino acid - Tyrosine.

Determination of blood Amino acid levels was carried out by gas chromatography with using an Thermo Fisher Scientific Trace 1600 apparatus.

All procedures performed within the study complied with the ethical standards of the ethics committee and the provisions of the Declaration of Helsinki.

Results

Clinical biochemistry is centered on the principle that all diseases have a biochemical basis and have a disturbances manifestation in the structure of molecules caused by the chemical reactions and processes. But not all biochemical reaction lead to changes in the primary structure of molecules. And not all partial changes in the transformation mechanism will cause disruptions in vital processes. At the same time, any disruptions in the normal functions of the organism are as results of metabolic processes at the molecular level. There are no diseases of molecules, but there are pathological conditions of the body that manifested themselves in function disruptions of individual organs or the entire child organism. We have considered the spectrum of the studied Amino acids (table 1).

Table 1

Investigation of the Amino acid spectrum of the blood serum in children with Acute Respiratory Viral infections

Parameters	Study group (n=60)	Control group (n=26)	Statistical significance of differences (p)
Tryptophan (25–99, mkmol/l)	39,74±10,53	57,48±7,11	p_1<0,001;
Alanine (188–624, mkmol/l)	294,65±64,68	430,27±55,81	p_1<0,001;
Glycine (111–426, mkmol/l)	228,62±47,65	315,38±43,28	p_1<0,001;
Methionine (12–32, mkmol/l)	19,04±3,33	26,25±4,19	p_1<0,001
Phenylalanine (28–80, mkmol/l)	46,47±8,80	56,40±6,93	p_1<0,001
Tyrosine (32,2–85, mkmol/l)	47,03±5,86	60,35±5,18	p_1<0,001

Notes: p1 – reliability of differences in group 1 between the values of indicators and indicators of the control group.

In general, changes are observed in the disease, caused by both the pathological process itself and the development of metabolic changes in the organism. This may include the follows: an increase or decrease in the content of substance; an increase or decrease in the activity of enzymes; the appearance of metabolites or abnormal forms that do not occur in a healthy person; an inadequate response to the load of certain substances and etc. For various pathological conditions (except for genetically determined ones), biochemical changes are not clearly specific, and therefore, such criteria as "more – less", "faster – slower", "presence – absence" of organ-specific indicators, isoenzymes, etc. are taken into account. Indicators are evaluated in comparison with indicators in healthy people, the degree of severity, the time of occurrence of changes in a particular indicator and the duration of the detected disorders are recorded [4].

We conducted a study of the Amino acid contens of blood serum in children with ARVI in accordance with the tasks of the investigation. We studied non-essential Amino acids (Alanine and Glycine), essential (Tryptophan, Methionine, Phenylalanine) and the conditionally essential Amino acid – Tyrosine. The levels of all studied Amino acids varied within the reference values and had significant differences compared to the data of the control group, in particular: Alanine (294.65±64.68 versus 430.27±55.81 μmol/l in comparation to the control group data, p1<0.001); Glycine (228.62±47.65 versus 315.38±43.28 μmol/l, p1<0.001); Tryptophan (39.74±10.53 versus 57.48±7.11 μmol/l, p1<0.001); Methionine (19.04±3.33 vs. 26.25±4.19 μmol/l, p1<0.001); Phenylalanine (46.47±8.80 vs. 56.40±6.93 μmol/l, p1<0.001); Tyrosine (47.03±5.86 vs. 60.35±5.18 μmol/l, p1<0.001).We have analyzed the main characteristics of the Amino acids under study. Phenylalanine is an essential amino acid, and its hydroxylation by phenylalanine hydroxylase (PAH) generates Tyrosine. Tyrosine can be formed from the metabolism of Phenylalanine and is necessary for the synthesis of Melanin and Catecholamines [5].

Tryptophan is an essential Amino acid that is both Ketogenic and Glucogenic because it can be oxidized to Alanine and Acetyl-CoA. The ring structure can also be used to synthesize Niacin, reducing the dietary requirement for this Vitamin [6].

Methionine is an essential Amino acid with a complex metabolism of important clinical significance. Its metabolism interacts with the Folate cycle, Cobalamin remethylation and S-adenosylmethionine (SAM) synthesis. Enzymatic or cofactor deficiency can lead to increased Homocysteine levels (hyperhomocysteinemia), which causes systemic negative effects. Methionine, which is required for SAM synthesis, comes from food or is synthesized during the remethylation of homocysteine with the participation of vitamin B12 synteses. The main biological functions of Methionine is next: Methyl group donor (methylation) via S-adenosylmethionine (SAMe), which is a key Methyl group donor for numerous biochemical reactions (synthesis of Nucleic acids, metabolites, hormones, membrane components); precursor of important compounds (Choline, Adrenaline, Creatinine, Taurine, Cysteine, as well as components of cell membranes, in particular Phospholipids); antioxidant promotes detoxification of the organism and synthesis of Glutathione; has a lipotropic effect: inhibits excessive fat accumulation in the Liver; helps to normalize the phospholipids and cholesterol level [7,8].

Alanine is the most easily synthesized Amino acid from pyruvate. A simple transamination catalyzed by Alanine transaminase yields Alanine from pyruvate. It participates in the glucose-alanine cycle and facilitating the removal of Ammonia from tissues. Alanine can serve as a substrate for glucose synthesis in the liver [9].

Glycine is the simplest Amino acid among the 20 standard Amino acids. Main functions are: a component of Protein synthesis, especially Collagen; acts as a Neurotransmitter in the CNS (has an inhibitory effect, reduces anxiety, helps regulate sleep); participates in the synthesis of Hemoglobin, Creatine, antioxidant Glutathione and Porphyrin pigment; contributes to cellular respiration indirectly, in particular through the following mechanisms: synthesis of Heme (Hemoglobin, Cytochrome), support of antioxidant protection (Glutathione, where Glycine is one of the three components abreast with Glutamate and Cysteine); synthesis of Creatine (Creatine → Phosphocreatine - a reserve source of energy in muscles and brain) [10,11].

Organs and tissues contain a somewhat of free Amino acids. After absorption, they enter through the portal system to the Liver, which is the main organ of Amino acid metabolism in the human organism. Peripheral tissues absorb Amino acids which circulating in the blood by different ways. The organism's free Amino acid pool is replenished due to the breakdown of tissue

proteins and the synthesis of replaceable amino acids in tissues, with the excepton of food Amino acids that enter the the body [12]. Part of the free Amino acids is involved in anabolic processes, i.e. used by various tissues for the synthesis of Enzymes, structural Proteins and physiologically active compounds of Protein and Peptide nature. Amino acidswhich dont participate in anabolic processes are involved in catabolic reactions. A certain part of the Nitrogen-free Carbon skeleton of Amino acids is involved in Gluconeogenesis (synthesis of Glucose from non-Carbohydrate compounds) and Ketogenesis (formation of Ketone bodies). Thus, the total pool of blood Amino acids is formed by flows that ensure the supply of free amino acids and their using in various anabolic and catabolic processes [13].

Amino acids are classified according to their catabolic pathways. There are three main categories: those that form intermediates in the Glycolytic pathway (Glycogenic); those that yield intermediates of Acetyl-CoA or Acetoacetate (Ketogenic); and mixed Amino acids that are both Glucogenic and Ketogenic. Amino acids largely form breakdown products related to intermediates of the Tricarboxylic Acid cycle (Krebs cycle) or Glycolysis, but this is not the complete picture. Some Amino acids, such as Tryptophan, Phenylalanine, and Tyrosine, are precursors of Hormones and Neurotransmitters in subsequent metabolism. Others, such as Cysteine and Methionine, are eliminated with the release of Sulfur. All Amino acids must get rid of Nitrogen, which occurs through the Urea cycle, Transamination, or a combination of these processes [11,12]. Amino acid metabolism and signaling processes are involved in the control of pathogenic infections and the regulation of inflammation caused by the activation of Innate, adaptive, and regulatory Immune responses. The interaction between Amino acid catabolism and the Immune system is an important mechanism for regulating Immune reactivity and limiting Hyperinflammation associated with Immune responses to infections. Some Amino acids are involved in the Innate inflammatory response through the formation of NO and implement Catabolic pathways that regulate Immune reactivity and influence the course of Inflammation and adaptive Immune responses [13].

Conclusions

The present study found Amino acid levels within reference ranges, but with significant decreases compared to control group data. In contrast, previous studies have shown that Amino acid excess creates conditions that perceived viral entry, while Amino acid lack and GCN2 activation prevent entry. Both mechanisms represent potential therapeutic targets for controlling infection and the associated hyperinflammatory response that contributes to pathogen-induced morbidity and mortality [12,13].

Conflict of interest: The authors report no conflict of interest.

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