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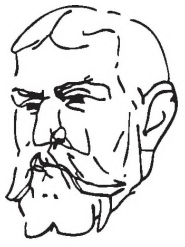

Memory of dr Władysław Biegański

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ORIGINAL ARTICLE

FEATURES OF DENTAL STATUS AND METABOLISM IN CHILDREN WITH EARLY CHILDHOOD CARIES AGAINST THE BACKGROUND OF CONNECTIVE TISSUE DYSPLASIA

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Iryna I. Sokolova, Olena H. Yaroshenko, Svitlana I. Herman, Tetiana V. Tomilina, Karyna V. Skydan, Maxym I. Skydan
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ABSTRACT

The aim: To assess the dental status of infants suffering from connective tissue dysplasia, with the analysis of some aspects of hydrocarbon and amino acid metabolism (blood, urine) and internal organs status.

Materials and methods: 81 infants (aged 14 – 36 months) with multiple dental caries were examined. Among them 39 infants were suffered from connective tissue dysplasia.

Results: High prevalence of caries in infants against the background of connective tissue dysplasia compared to their peers in the control group ($p < 0.05$) is established: the caries intensity index and the caries intensity growth index are high in all age groups. Disorders of amino acid and carbohydrate metabolism were observed in infants of the main group. Thus, simultaneous increase of amino acids in the blood and urine was observed in 34 children of the main group in different age groups, and simultaneous increase of amino acids in the blood and urine and carbohydrates in the urine was observed in 25 children in different age groups. In infants of the main group the ultrasound examination of abdominal organs revealed changes in the liver, gallbladder, spleen, pancreas and kidneys.

Conclusions: When carrying out endogenous prophylaxis of dental caries in infants with connective tissue dysplasia, it is necessary to take into account the internal organs' status and thin-layer chromatography data of amino acids and carbohydrates in the blood and urine and to prescribe peroral drugs together with the doctors geneticists.

KEY WORDS: connective tissue dysplasia, infants, caries, level of hygiene, amino acid metabolism

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INTRODUCTION

It's well known that children are the most vulnerable part of population [1]. It has been proved by many investigations that dental health is also highly influenced by geochemical condition of the region, somatic health, psychological status of the children and heredity [2, 3].

Hereditary amino acid metabolism occupies a special place in a wide range of genetically determined childhood pathologies [4-6]. This group of pathology is common and it is possibly due to the complexity of the protein metabolism biochemical organization, which also involves amino acids, that the probability of various metabolism units disruption is growing [7, 8].

In patients with congenital "metabolism error" there is a primary enzymatic defect and there is an increase in the level of one or more amino acids (AA) in the blood and / or urine, which leads to multiple disorders in functions of various organs and systems [9, 10]. Excess levels of AA or their metabolites cause toxic effects on the body and cause severe clinical disorders [11].

The connective tissue in the human body occupies a special place and is present in all organs and systems, accounting for more than 50% of the body weight. Most of the tissues in the maxillofacial area have also connective tissue origin. Connective tissue dysplasia (CTD) is a condition that is caused by structural changes in individual components of the connective tissue as a result of disorders in the embryogenesis process. CTD is a systemic process that is the basis for the development of pathology.

First of all, CTD is the basis of many structural and shaping changes in organs and systems that determine dysplastic-dependent disorders of functions [12-15]. Dysplastic-dependent changes in the internal organs are of greatest interest to researchers, as they determine the prognosis for the patients' lives. The presence of a "defective" connective tissue alters and reduces the body's ability to adapt when exposed to adverse environmental factors or changes in the conditions of the body's existence.

Many authors believe that the generalized form of CTD is more common. The main markers are changes in the valvular heart apparatus, hypermobility of the joints, pathology of the musculoskeletal system, skin hyperelasticity, anomalies in the structure of internal organs [6, 7].

Taking into account that different disorders of formation depend on the connective tissue condition in the body as a whole [7, 8], as well as following the principle of structural and functional unity of organs and tissues and given the high prevalence of connective tissue pathology, the study of its effect on the condition of hard of tooth tissue in younger children is relevant and timely.

Table I. Indices of the hard tooth tissues and oral hygiene status in infants against the background of CTD.

Age of infants, months	14-18		19-23		24-29		30-36	
Number of infants in groups, n	Control group	Main group	Control group	Main group	Control group	Main group	Control group	Main group
	10	7	12	8	7	7	13	17
Number of teeth in oral cavity, n	10.00± 0.96	10.00± 1.12	14.3± 1.38	14.00± 1.39	17.14± 0.27	17.14± 0.18	20.00± 0.00	20.00± 0.00
Index CF, points	1.7± 0.42	3.00± 0.92*	2.25± 0.41	3.00± 0.92*	3.27± 0.92	5.14± 1.80*	3.37± 0.85	6.29± 0.50*
CIGI index, points	0.15± 0.03	2.25± 0.59	0.15± 0.02	2.08± 0.59*	0.18± 0.04	2.34± 0.83*	0.16± 0.04	2.27± 1.18*
Carious teeth in oral cavity, %	15.64± 3.38	30.24± 4.83*	14.91± 2.09	22.83± 4.14*	19.2± 4.46	36.30± 9.35*	16.5± 4.26	33.0± 4.83*
Number of teeth with complicated caries (P and Pt), n	0	0	0	2.0± 0.0	0	2.41± 0.64	0	2.51± 0.89
Teeth health index (THI), points	0.04± 0.67	0.51± 0.04*	0.14± 0.02	0.49± 0.10*	0.11± 0.03	0.64± 0.13*	0.12± 0.04	0.59± 0.06*
Index interpretation	good	poor	satisfactory	poor	satisfactory	poor	satisfactory	poor

Notes: * – statistical difference between the main and the control groups.

Table II. Number of infants with CTD who have changes in abdominal organs.

Age of infants with CND	Number of infants	Number of infants with changes in				
		liver	gallbladder	pancreas	spleen	kidneys
14-18 months	7	7	7	2	1	6
19-23 months	8	8	8	3	2	7
24-29 months	7	7	7	6	1	7
30-36 months	17	17	17	11	2	15
Total	39	39	39	22	6	35

THE AIM

The aim of our study was to assess the dental status of infants suffering from connective tissue dysplasia, with the analysis of some aspects of hydrocarbon and amino acid metabolism (blood, urine) and internal organs status.

MATERIALS AND METHODS

The survey included 81 infants (aged from 14 to 36 months). The children were divided into two groups: the main and the control ones. The main group included 39 infants with multiple caries against the background of CTD. At the Department of Genetics and Prenatal Diagnosis of KhNMU (Doctor of Medical Sciences, Prof. O.Ya. Grechanyna), these infants were studied for the blood and urine carbohydrates and amino acids by means of thin layer chromatography (TLC) and ultrasound (U/S) diagnostics of internal organs. The diagnosis of "connective tissue dysplasia" was established by a geneticist for a selected contingent of infants. The control group included 42 infants of the similar age who were somatically healthy but had carious dental lesions.

All children were divided into four age groups, depending on the number of incised teeth. Thus, the first group included 7 infants in the main group and 10 in the control one at the age of 14 – 18 months, the second group – 8 infants in the main group and 12 in the control one at the age of 19 – 23 months, the third group included 7 infants in the main group and 7 – in the control at the age of 24 – 29 months, and finally the fourth group – 17 infants in the main group and 13-in the control at the age of 30 – 36 months.

The study was carried out in compliance with the basic bioethical standards of the World Health Association's Helsinki Declaration on Ethical Principles for Scientific and Medical Research and its materials were reviewed by the local Ethics and Bioethics Committee of Kharkiv National Medical University. Written informed consent was obtained from all participants (parents of infants).

All infants were determined their Temporal Tooth Caries Intensity Index (CF), the Temporal Tooth Caries Intensity Growth Index (CIGI) [16]. Additionally, all infants were assessed for hygienic condition of the oral cavity using the teeth health index (THI) according to the method of E.M. Kuzmina [17].

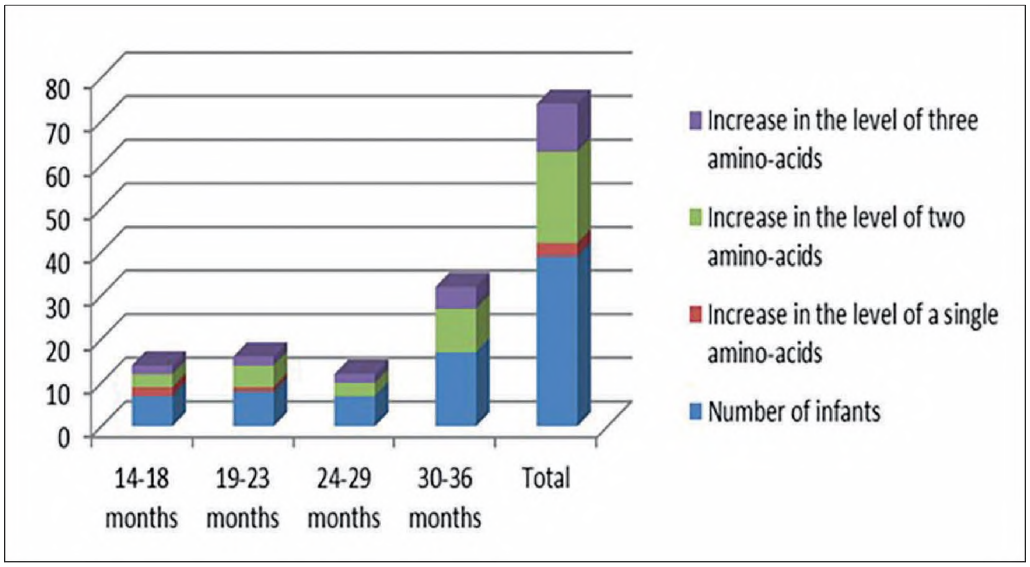

Fig 1. Amount of amino acids in the blood of the main group infants whose level is increased.

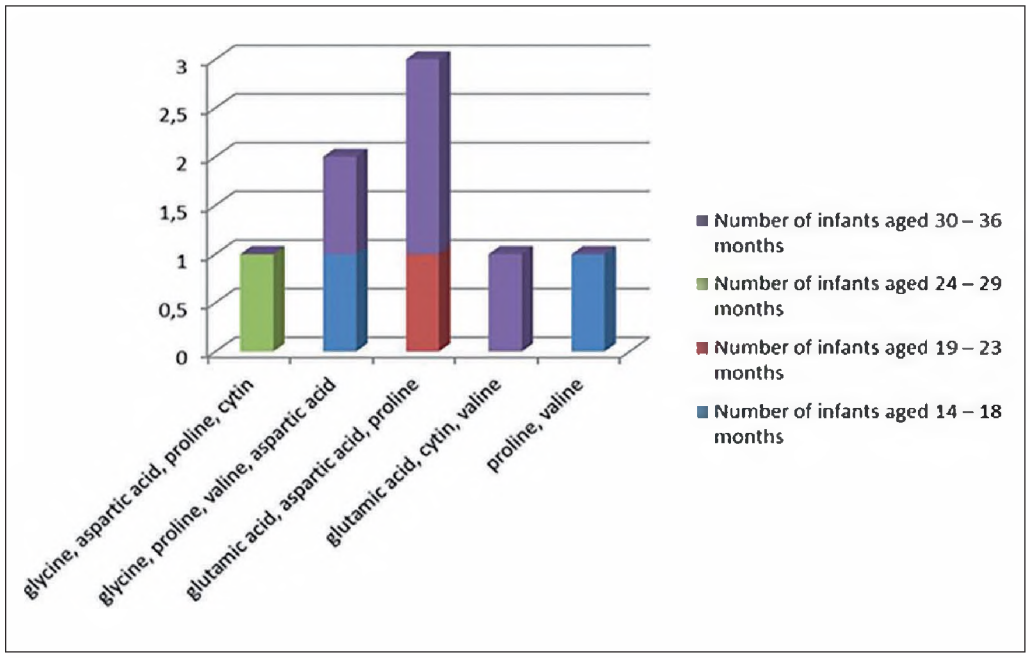

Fig 2. Increased amino acids level in the main group infants' urine.

RESULTS

The results of the studies indicate a high prevalence of caries in infants against the background of CTD. The caries intensity index (CF) is very high at all ages, and the caries intensity growth index (CIGI) is also high. As a result of the oral hygiene study in the selected contingent of infants, a high index of plaque was established, which indicates poor oral hygiene. All data are presented in table I.

As it can be seen from the data in table 1, the caries intensity index (CF) of temporary teeth has a very high level in infants of both the main and the control groups, especially in infants aged from 24 to 36 months. Besides, in all children with CTD, the index values were higher than those in children without the above pathology of amino acid metabolism. Thus, in infants aged 14-18 months, the intensity of caries was by 1.8 times higher than that in the control group ($p = 1.285$); in infants aged 19-23 months – by 1.3 times ($p = 0.744$); in infants aged 24-29 months – by 1.6 times ($p = 0.925$) and in those aged 30-36 months – by 1.9 times ($p = 2.961$) (table I).

The CIGI index for temporary teeth up to 0.4 points is considered low, from 0.5 to 0.8 points – average, from 0.9 to 1.2 points – high and above 1.3 points – very high. According to table 1, the CIGI index in infants of the main group aged 14-18 months is higher than that in infants of the control group by 15 times ($p = 3,554$); in infants aged 19-23 months – by 13.8 times ($p = 3.369$); in infants at the age of 24-29 months – by 13 times ($p = 2.599$) and in those at the age of 30-36 months – by 14.1 times ($p = 1.787$). Therefore, the CIGI index in the surveyed infants of the main group was on average by 1.7 times higher than the very high level of this index ($p < 0.05$) (table I).

The percentage of carious teeth in the main group infants aged 1 to 36 months was 30.59±5.58%, which is by 1.8 times

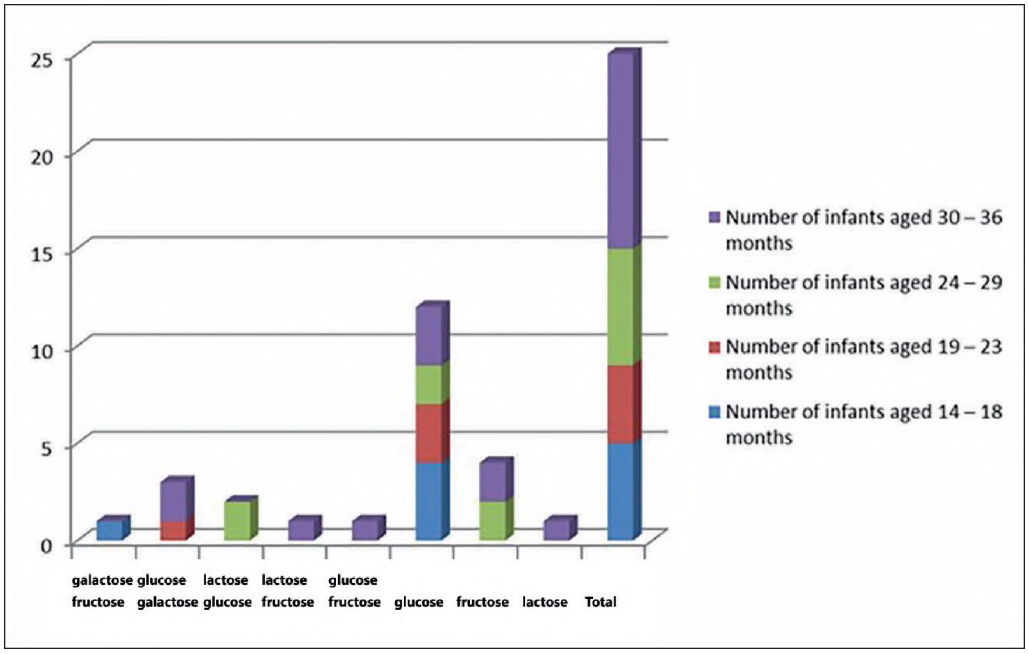

Fig 3. Increased carbohydrates level in the urine of the main group infants.

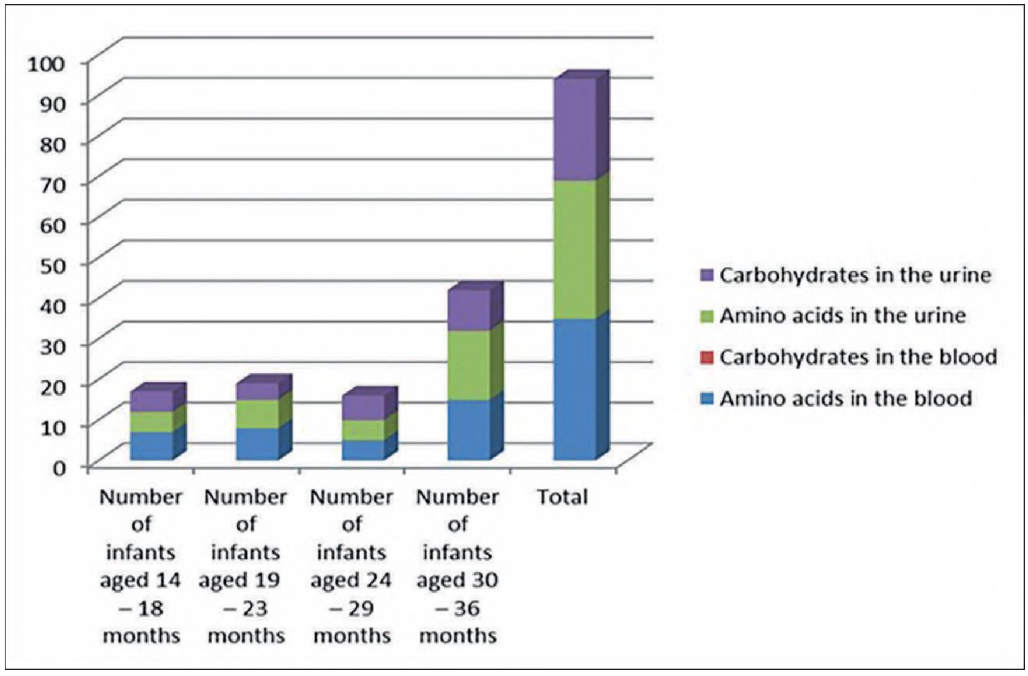

Fig 4. The number of children in the main group with a simultaneous increase in the level of amino acids and carbohydrates in the blood and urine.

higher than that in the control group (p = 2.476). Also in the main group of age categories such as 19-23, 24 -29 and 30-36 months there are already teeth lesions with chronic forms of pulpitis and periodontitis (table I).

With regard to oral hygiene, the main group infants of all ages were found to have its poor level (p <0.05). But it should be noted that in infants of the control group the level of oral hygiene is good only in the first age period, and in the last three age periods it was satisfactory (table I).

Also at the Department of Genetics and Prenatal Diagnosis of KhNMU, children with CTD were performed thin-layer chromatography (TLC) of the blood and urine amino acids and carbohydrates of (data are presented in fig.1, fig.2, fig.3, fig.4 and table II).

Data of the TLC studies on the blood amino acids in the main group infants indicate that 36 infants out of 39 showed an increase in amino acid levels (fig. 1). Thus, the level increase in a single amino acid in the blood (aspartic acid and glycine) was observed in three infants. A simultaneous increase in the level of two amino acids in the blood was observed in 21 infants. Increase in the level of two amino acids was in the folloing combination: glycine and glutamic acid; glycine and aspartic acid; glycine and proline; glycine and alanine; glutamic acid and aspartic acid; glutamic acid and alanine; aspartic acid and proline; aspartic acid and alanine; aspartic acid and valine; proline and alanine; proline and valine.

A simultaneous increase in the level of three amino acids in the blood was found in 11 infants. The increased amino

acids were in the following combination: glycine, proline, alanine; glycine, proline, valine; glutamic acid, aspartic acid, alanine; glycine, aspartic acid, proline.

An increase of the carbohydrates level in the blood was not observed.

With regard to amino acids in the urine (fig. 2), the result of the analysis indicates a simultaneous increase in their quantitative and variational indices. Thus, an increase in the levels of four amino acids such as glycine, aspartic acid, proline and cytin was observed in one infant in the third age period (24-29 months). An increase of four amino acids, but in another combination (glycine, proline, valine, aspartic acid) was observed in two infants in the first (14 18 months) and fourth (30 – 36 months) age periods. An increase in another combination of four amino acids (glutamic acid, aspartic acid, proline, valine) was observed in one child of the second age group (19-23 months) and two children of the fourth age group (30 – 36 months). An increase of three amino acids (glutamic acid, cytin, valine) was observed in one child of the fourth age group (30 – 36 months) and an increase of two amino acids (proline, valine) was observed in one child of the first age group (14-18 months) (fig.2).

The next item to be analyzed was the level of carbohydrates in the urine (fig. 3). We found that in the first age period (14-18 months) the increase in carbohydrate level was observed in five infants, in the second age period (19-23 months) – in four infants, in the third age period (24-29 months) – in six infants and in the fourth age period (30 -36 months) – in ten infants. Carbohydrates, the level of which was increased in the urine, were fructose, galactose, glucose, lactose (fig. 3).

Elevation of carbohydrates level in the urine of the main group patients was observed in 15 infants.

Therefore, changes in the urine were observed in all the 39 children of the main group and were manifested in an increase in the amino acids and carbohydrates level.

It should be noted additionally, that we also found a simultaneous increase in amino acids in the blood and urine observed in 34 children of different age groups, and a simultaneous increase in amino acids in the blood and urine, and carbohydrates in the urine observed in 25 infants of different age groups (fig. 4).

During the ultrasound examination of abdominal organs in infants with CTD changes were observed in the liver, gallbladder, pancreas, spleen and kidneys (table II).

As it is seen from table II, changes in the liver and gallbladder condition were observed in all the 39 infants suffering from CTD. The second place in the incidence of the changes detected during ultrasound study is occupied by the kidneys (35 infants out of 39), the third – by the pancreas (22 infants out of 39) and, finally, the last position belongs to the spleen (6 infants out of 39).

According to the ultrasound study, changes in the liver were manifested in the form of venous plethora, perivascular infiltration, moderate diffuse changes. Condition of the bile ducts was characterized by the presence of diffuse changes, bending of the gallbladder, hypotension; condition of pancreas and spleen – presence of reactive changes; and the state of the kidneys – by the presence of completely dysplastic metabolic changes, perivascular infiltration, pyelectasis of one or two kidneys.

DISCUSSION

Thus, our data on disorders of amino acid and carbohydrate metabolism indicate a significant disorder of metabolism, which is a symptom of some genetically determined connective tissue diseases, including connective tissue dysplasia [6, 10, 12].

In general, the results of our studies coincide with the opinion of other researchers on disorders of amino acid metabolism in hereditary connective tissue diseases. Thus, according to Smolnova TYu, Adamyan LV. (2013) the impairment of amino acid biosynthesis is the leading link in the formation of pathology of intermediate metabolism [13]. When the transport of amino acids is disturbed, various forms of genetically determined diseases can be observed – from asymptomatic to those with severe clinical manifestations. And the basis of increased excretion of amino acids in the urine, as a rule, is an impairment of tissue metabolism of amino acids or their transport at the level of cell membranes in the renal tubules [7].

The importance of amino acids in the metabolism of the human body is difficult to overestimate. Thus, alanine, aspartic acid, glutamic acid, proline, glycine – are substituted amino acids and in the biosynthesis of substituted amino acids, their carbohydrate part is formed from intermediates of glucose oxidation, which can affect carbohydrate metabolism. This is confirmed by the results of our studies and this coincides with the opinion of Hrechanina O.Ya. et al. [9]. Aspartic and glutamic amino acids are important in the body's metabolism, participating in the processes of protein biosynthesis, the formation of other amino acids. Alanine is a part of muscle extractives. «Conditionally substitutable» acids include cystine, glycine, which are also involved in most biochemical processes in the body. In particular, glycine is involved in the synthesis of the most important substances for the body – nucleic acids. Also, these amino acids are part of proteinoids – simple proteins that are part of the supporting tissues, collagen [12].

The amino acids mentioned are glucogenic, i.e. those that give their carbohydrate fragments for the formation of carbohydrates. And as you know, carbohydrates, which are part of mucopolysaccharides, perform structural, protective and regulatory functions. Thus, mucopolysaccharides make up the bulk of extracellular tissue, are part of the skin, cartilage, synovial fluid [7, 9, 11]. The importance of amino acid metabolism in the development of genetically determined connective tissue pathology is also emphasized by such geneticists as Nikolayev KYu, Oteva EA, Nikolayeva AA, BugayevaYeV, Vasilyeva OV, Korenev NM [4, 6, 8].

The importance of carbohydrate metabolism in connective tissue pathology is also based on the fact

that they directly affect the formation of phosphorus compounds. Thus, metabolism of calcium and phosphorus in the body is regulated by calcitonin – a peptide consisting of a chain of amino acid residues [12,13].

Castori M. et al. concluded that an increase in the level of one or more amino acids in the blood and/or urine can lead to multiple dysfunction of various organs and systems [14]. The works of other researchers suggest that as a result of mutations in the regulatory or structural gene, amino acids or their metabolites accumulate, which causes toxic effects on the body [15-17].

Today, the most common is to determine the level of amino acids in the daily sample of urine or blood serum. All of these are markers of collagen breakdown, which are considered to be objective and accurate criteria for connective tissue dysplasia (CTD). Therefore, determination of the level of amino acids in the daily sample of urine or blood serum can be used both for the purpose of diagnosis and for control of further rehabilitation. This is confirmed by the results of our study, as well as the work of other scientists [12, 15].

Therefore, analyzing the known data on the occurrence of disorders of amino acid and carbohydrate metabolism in patients with connective tissue dysplasia, we can conclude that it is appropriate to further study these pathogenetic aspects in order to timely identify risk groups for possible complications.

CONCLUSIONS

1. In the main group infants with poor cf (3) and high levels of caries intensity growth index (CIGI), poor oral hygiene is observed.
2. In young children, high levels of dental caries intensity and its growth, high rates of plaque deposition may be both a consequence of connective tissue dysplasia and one of its first clinical manifestations.
3. In infants with multiple lesions of the teeth against the background of CTD impaired amino acid metabolism was observed, which was detected during the TLC of carbohydrates and amino acids in the blood and urine. During ultrasound examination of the abdominal organs, changes in the liver, gallbladder, spleen, pancreas and kidneys were detected.
4. In infants with CTD and the presence of complicated caries in the oral cavity, a foci of chronic infection may be formed, which may further enhance the impact of the pathological factor in the presence of dysplastic changes in the liver and kidneys.
5. When carrying out endogenous prophylaxis of dental caries in infants with CTD, it is necessary to take into account the internal organs' status and TLC data of amino acids and carbohydrates in the blood and urine and to prescribe peroral drugs together with the doctors geneticists.
6. For infants with CTD it is necessary to develop and carry out individual methods of exogenous prevention of the dental caries development.

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