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DENTAL STATUS AND DIAGNOSIS OF CHILDREN AND ADOLESCENTS SUFFERING FROM VARIOUS FORMS OF CONNECTIVE TISSUE DYSPLASIA

Gafforov SunnatulloAmruloevich
Center for the Development of Professional Qualifications of Medical Workers Under the Ministry of Health of the Republic of Uzbekistan.

Shaymatova Azizakhon Rustambekovna
Center for the Development of Professional Qualifications of Medical Workers Under the Ministry of Health of the Republic of Uzbekistan.

ANNOTATION

The study is based on retrospective and prospective data obtained because of observation of patients in 2020-2022 with varying degrees of connective tissue dysplasia (DCT) who were under dispensary supervision in the departments of the screening center and patients who sought dental care with diagnoses of "differentiated and undifferentiated connective tissue dysplasia". In the course of research, the authors obtained data that allow us to conclude that the mechanism of bone desorption of the alveolar process in adolescent patients with DCT pathologies is a violation of the bone remodeling cycle against the background of an imbalance of calcium-regulating hormones, while a decrease in the rate of bone formation against the background of a normal level of bone desorption is the cause of the pathology of teeth and periodontal tissues.

Keywords: Connective tissue dysplasia, osteogenesis imperfecta, Marfan syndrome, metabolic disorders.

INFORMATION ABOUT THE AUTHORS:

Shaimatova A. R. -https://orcid.org/0000-0001-7748-809X.
Автор, ответственный за переписку: azizarustambekovna@gmail.com

RELEVANCE

Connective tissue, which occupies 50-80% of body weight, plays a special role in the human body. It performs 5 major functions: biomechanical, trophic, barrier, plastic and morphogenetic.Today, differentiated and undifferentiated connective dysplasia (DCTD and UDCTD) are distinguished [2, 17,18].DCTD is characterized by a certain type of inheritance, a distinct clinical picture, often established and well-studied genetic and / or biochemical defects such as Marfan, Ehlers-Danlos, Alport syndromes, imperfect osteogenesis-bullous form of epidermolysis and others;UDCTD- is diagnosed when a set of phenotypic and other signs in a patient does not fit into any of the differentiated diseases.Despite numerous publications devoted to problems with DCTD pathologies, the issue of assessing and providing specific dental care to such patients remains open, especially among children and adolescents who often seek dental care[11, 12, 13, 14]. Also, there are literary sources describing the features of multifactorial CTD in young children, multiple organ disorders in them from the cardiovascular

(CV), respiratory, urinary systems, gastrointestinal tract (GIT), hemostasis, central nervous system (CNS), musculoskeletal systems, ENT organs and dentoalveolar system (DAS)[4, 9,17] In recent years, there is often scientific research on the increase in the number of pathological conditions associated with CTD[5, 10]. Also, it is known about the undoubted importance of the role of CTD, which is the morphological basis for the formation of anomalies in the development of the musculoskeletal and ventricular system [6, 9], the cause of various disorders of the central nervous system and visceral organs[1, 3]. It should be noted that there are few studies devoted to the study of the characteristics of the manifestations of CTD in the maxillofacial region (MFR) in children, as well as the role of dysplasia in the development of anomalies in the development of the MFR in childhood.In most cases, the formation of dentoalveolar anomalies and deformities (DAA and DAD) in children is the result of a complex interaction of many factors that affect the growth and development of DAS[15, 16]. The effectiveness of correcting the development of the maxillofacial region (MFR) depends on timely diagnosis and the correct choice of therapeutic and preventive measures.Therefore, it is necessary to study the connective tissue system, which determines the morphological and functional integrity of the body, affected in various acute and chronic pathological conditions.

The aim of the study was: Evaluation of the frequency and occurrence of dental pathology in children and adolescents suffering from various forms of CTD, as well as determine the features of the clinical diagnosis of MFR.

MATERIALS AND RESEARCH METHODS

The study is based on retrospective data obtained as a result of observation of patients in 2020-2022 with different severity of CTD, who were under dispensary observation at the screening center.We examined and studied some data from dispensary cards with hereditary CTD - 92, including those with a diagnosis of DCTD - 59 people (group 1); of them with Marfan syndromes - 14 (1a-group), Ehlers-Danlos - 12 (1b-group), Alport - 11 (1c-group), imperfect osteogenesis - 11 (1d-group), bullous form of epidermolysis - 11 (1e -Group); with UDCTD - 33 (group 2) and 32 practically healthy individuals without signs of musculoskeletal dysplasia (control group - C/G) aged 6 to 19 years (table No. 1).

Table No. 1. Characteristics of those examined with CTD pathologies and the control group by age (M + n in %)

Diagnosisandgroups			Age (M+nin %)		
			6-9years old	10-13 yearsold	14-18 yearsold
Examinedwith CTD 92/100%	DCTD (1-group) 59/64.1%	Marfansyndromes (group 1a) 14/23.7%	4/28,6	5/35,7	5/35,7
		Ehlers-Danlos (1b-group) 12/20.3%	3/25,0	5/35,7	4/33,3
		Alporta (1c-group) 11/18.6%	4/36,4	4/36,4	3/27,3
		imperfectosteogenesis (1d-group) 11/18.6%	3/27,3	3/27,3	5/45,5
		bullous form of epidermolysis (1d-group) 11/18.6%	3/27,3	4/36,4	4/36,4
		Medium: DCTD 59/64.1%	17/28,9	21/35,6	21/35,6
	UDCTD 33/35,8%		9/27,3	9/27,3	15/45,5
Totalexamined 124/100%		ExaminedwithCTD 92/74.2%	26/28,3	30/32,6	36/39,1
		Controlgroup 32/25.8%	7/21,8	12/37,5	13/40,6
Total 124/100%			33/26,6	42/33,9	49/39,5

The diagnoses were based on the results of retrospective and prospective data; study of the patient's medical documents, questioning the patient; general clinical - general examination; instrumental, biochemical, chemiluminescent methods.All examined were consulted by a geneticist to exclude chromosomal pathology, which was confirmed by a karyotype study.Also, in accordance with the classification proposed by Yakovlev V.M., Nechaeva G.I. (2008), all signs of dysplastic-dependent changes in organs and systems were divided into: locomotor, skin symptoms, visceral:In addition, microsigns of disturbed morphogenesis were revealed - for example, widely spaced palpebral fissures; antimongoloid incision of the eyes; arched sky; gothic sky; uneven row of teeth; central diastema; malocclusion; frenulum of the upper lip and others.Also, in order to verify the phenotypic signs of CTD, various anthropometric methods were used.An important point for differential diagnosis was the collection and compilation of a genealogical anamnesis of families; from relatives of probands and healthy individuals were obtained by questioning, if possible, during a direct examination of relatives, as well as during the analysis of their medical records.

In order to assess bone mineral density (BMD) tissue - BMD of trabecular and cortical bone tissue was assessed using computed tomography: for this, all patients underwent X-ray (R) densitometry on a densitometer in the region of the lumbar spine at the level L-L_4 and proximal sections femurs on the right and left; the criteria were such indicators as the bone mineral component - the amount of mineralized tissue during bone scanning; Tissue BMD - the amount of mineralized bone in the scanned area and to evaluate the use of the T-test [7, 8]. In order to assess the mineral metabolism and bone restructuring - bone formation and bone resorption in C/G, 10 boys and girls, all underwent a study of mineral and bone metabolism.

All patients underwent general clinical studies; complete blood count and urinalysis, biochemical and laboratory diagnostics were carried out on the analyzer.Also, the concentrations of magnesium (Mg), Ca, inorganic P, alkaline phosphatase (AP) activity in the blood serum without traces of hemolysis were determined.The normal values of the total Ca content in the blood serum in adults are - 2.25-2.75 mmol/l, the concentration of Mg - 0.74-1.2 mmol/l, inorganic P - 0.87-1.45 mmol/l .For the level of Ca and P in the urine with normal concentration values, the amount for inorganic P -13-42 mmol/24 hours, - Ca - 2.5-7.5 mmol/24 hours was used.

In dental methods for assessing the state of hard tissues of teeth and periodontium, parameters of various indicators were used, taking into account the requirements of the International Protocol for assessing the severity of periodontal diseases [18], including the following indices: CFE index - the number of caries-affected (C), filled (F) and extracted teeth (E), the calculation of the index and the level of caries intensity were characterized according to WHO recommendations: 0-1.5 - very low intensity; 1.6-6.2 - low; 6.3-12.7 - medium; 12.8-16.2 - high and more than 16.2 - very high: the diagnosis - pathology of periodontal tissue was put on the basis of ICD 10-C according to K05.31

The R-methods of the jawbones were carried out on an orthopantomograph (OP) and a quantitative assessment of the degree of resorption of the alveolar part of the lower jaw (l/j) and the alveolar process of the upper jaw (u/j) used the indices of destruction of the alveolar bone - the Fuchs index and the R-cue index.The MCI index was used to quantitatively and qualitatively characterize the l/j cortical layer.[17]

To assess the statistical significance of the results of the study, expressed by quantitative characteristics, analysis of variance was used, as well as an assessment of the statistical significance of the difference in group means, using Fisher's test (F-test) when comparing more than two groups, Student's test (t-test), to compare mean values, the results of the analysis were considered statistical, with the probability of error not exceeding 5% ($p < 0.05$).

RESULTS AND ITS DISCUSSION

As can be seen from the results obtained, according to the dental condition in the studied groups: in the 1st group - patients with DDST, the intensity of caries was average -9.1 ± 0.6; ratio of CFE elements, C -3.0±0.2; F -4.7±0.5; E -4.9±0.2 out of a total of 16.5±0.6 teeth, while non-carious damage to the teeth was -7.9±0.4, pathology of periodontal tissues -71.4±0.5.From the 1st group of patients, a high rate of dental problems is observed with periodontal tissues (72.4±0.8) in the 1a group (Marfan's syndromes); high rates of caries intensity (9.9±0.3) and non-carious lesions of hard tissues of the tooth (9.8±0.8) among patients of the 1d group (osteogenesis imperfecta); among patients of the 2nd group, the above dental lesion is noted 60.4±1;2; 3.2±0.4 and 7.4±0.4, respectively, while dental pathologies are less significant in C/G.

Table No. 2. Indicators of carious lesions and diseases of periodontal tissues in patients with CTD.

Diagnosisandgroupsin %.		Intensityofcaries	SpecificGravity CFE				Non-carious lesions of the teeth	Periodontaldisease
			C	F	E	TotalTeeth		
1 gr; DCTD 59/64,1%	1a group 14/23,7%	8,1±0,8	2,1±0,9	6,7±0,2	2,2±0,6	16,8±0,7	6,0±0,6	72,4±0,8
	1b group 12/20,3%	9,4±0,3	2,8±0,4	5,6±0,4	3,4±0,9	17,4±0,8	6,8±0,8	72,8±0,2
	1c group 11/18,6%	9,8±0,5	3,6±0,8	4,8±0,8	6,0±0,8	14,8±0,4	8,4±0,4	66,4±0,8
	1d group 11/18,6%	9,9±0,3	3,8±0,8	4,0±0,4	8,2±0,4	15,4±0,6	9,8±0,8	68,8±0,6
	1e group 11/18,6%	8,4±0,4	2,6±0,4	2,6±0,4	4,6±0,8	17,9±0,9	8,6±0,2	76,8±0,4
	Average: DCTD 59/64,1%	9,1±0,6	3,0±0,2	4,7±0,5	4,9±0,2	16,5±0,6	7,9±0,4	71,4±0,5
2-гр; НДДСТ 33/35,8%		7,4±0,4	2,0±0,6	8,8±0,4	2,4±0,6	18,4±0,6	3,2±0,4	60,4±1,2
Average for CTD 92/74,2%		8,2±0,5	2,5±0,4	6,6±0,4	3,6±0,9	17,4±0,6	5,1±0,4	65,5±0,8
C/G - 32/25,8%		6,1±0,9	1,4±0,6	6,4±0,8	1,5±0,7	18,8±0,8	4,0±0,4	55,4±1,4
Survey average124/100%		7,2±0,5	2,9±0,5	7,3±0,5	2,5±0,7	18,2±0,6	4,1±0,4	60,4±1,1

Appendix: 1-group - DCTD; 1a-group - Marfan's syndrome; group 1b - Ehlers-Danlos syndrome; 1c - Alport's syndrome; 1d - imperfect osteogenesis; 1e - bullous form of epidermolysis; 2-group - UDCTD; C/G-control group.

For comparison, the main quantitative indicators of mineral metabolism and regulatory hormones in practically healthy boys and girls aged 14-18 years, the results showed that the content is Ca -2.22±0.22 mmol/l; P -1.56±0.42 mmol/l and Mg -0.88±0.08 in blood and P in urine - 32.4±2.22 mol/l are in practically healthy individuals.Hormonal indicators - somatotropic

hormone -3.8±0.18 mg/ml; ACTH -12.26±1.2 pg/ml; cortisol -440±24 nmol/ml; thyroid-stimulating hormone -1.49±0.4 mIU/ml; triiodothyronine -1.28±0.1 nmol/l; thyroxine -45.45±3.48 nmol/ml; prolactin -332±23 mIU/ml; parathyroid hormone -27.38±2.72 pg/ml: Biochemical markers of metabolism; ALP -78.04±6.6 units/l; osteocalcin -8.6±1.4 ng/ml; deoxypyridinoline in urine -4.2±0.41 mol/creatinine per day; Ca in urine - 3.14±0.8 mmol/day; homocysteine in blood plasma 12.38±0.04 μmol/l.

According to the results of the study of the BMD: R-th index and the determination of the Fuchs bone number, the Fuchs index in patients of the 1st group averaged 0.52±0.03, in patients of the 2nd group it was 0.58±0.08 which correspond to the degree of bone resorption of the alveolar part within 1/3 of the root length.At the same time, the value of bone tissue loss according to the R-th index turned out to be 1.34±0.04, which is 46% of the decrease in the total height of the alveolar process.The value of resorption of the bone tissue of the alveolar process in the u/j in patients of the 1st group was 1.26±0.24 (52%), which turned out to be higher than the indicator for the l/j 1.12±0.04 (45%) (p> 0.2).The value of the Fuchs index, which determines the level of resorption, turned out to be almost the same on average (p>0.5) in both jaws.In order to study the features of bone tissue resorption of the alveolar part of the jaws, in patients with different age groups, a comparative assessment of the state of the bone tissue was carried out, and there is a high sensitivity of the bone tissue to various external and internal influences, for example, a decrease in the functional load due to inflammatory periodontal diseases or hormonal disorders. regulation of mineral metabolism, especially for patients of groups 1a and 1b.The degree of loss of bone tissue of the alveolar process in the u/j practically did not depend on the age of the patients in the C/G, in contrast to the l/j, at 14-18 years, the level of resorption of the alveolar part was 0.18±0.04 (up to 1/4 of the length root), which is almost 2 times lower than the Fuchs index from the 1st (1a, 1b) and 2nd groups up to 14 years old 0.80±0.04 (up to 1/2 of the root length) (p <0.005).Analysis of the R-results of all groups confirms that the level of resorption of osteotropic hormones in patients with early onset CGP, the effect of which increases bone loss and reduces BMD.Thus, the analysis of R-data of patients with CTD pathologies - the loss of bone tissue of the alveolar bone is more active, especially in the horizontal type, mainly in the area of the interalveolar septa, while in patients C/G with chronic pathology of periodontal tissues, the vertical nature of resorption predominates with the formation of bone pockets.

In the results obtained, according to the effect on the mineral metabolism of other hormones in the 2nd group, depending on age and gender, we carried out an analytical assessment of the hormonal profile.Mean values in patients C/G somatotropic hormone -3.08±0.24 ng/ml; ACTH -15.24±0.42 pg/ml; cortisol -490.0±22.12 nmol/l; thyroid-stimulating hormone -1.80±0.42 mIU/ml; triiodothyronine -1.82±0.18 Nmol/l; thyroxine -86.63±1.22 nmol/l; prolacgin-242.6±10.9 mIU/ml; parathyroid hormone -37.45±1.12 (pg/ml): in patients with CTD in the age group of 18-20 years were significantly higher -2.14; -18.24; -438.0; -1.72; -1.62; -96.45; -262.2; -44.29 respectively, when compared with C/G (p<0.05).The absence of a hormonal shift in C/G is due to the completed biological growth in both sexes.

The results of studying the age characteristics of the level of homocysteine in the blood plasma of patients with UDCTD in patients aged 10-13 years -17.3±0.16 μmol/l; at the age of 14-18 years -20.55±0.12 μmol/l, while in C/G it was 10±0.14 (P2.3<0.05). This indicates that there

were no evidentiary differences between the reference limits of its fluctuations in the 2nd and 3rd age groups (p>0.05).

The results of a comparative assessment of the concentration of homocysteine in the blood plasma in patients with Marfan syndrome (group 1a) - in boys -40.22±0.2*; in girls -26.35±0.24; with UDCTD (group 2) in boys -26.46±0.41*; in girls -18.44±0.42, while in patients K/G - 11.8±0.44 (*-p<0.05).A comparative analysis of the level of homocysteine in blood plasma in men and women showed that the highest concentration was determined in boys with Marfan syndrome.The reference limits of homocysteine fluctuations in men were significantly higher than in girls of this group, as well as in patients of the 2nd group.It is possible that high concentrations of homocysteine in patients of the 1a group are mainly due to the type of inheritance, that is, homozygous insufficiency of the enzyme cystathionine-3-synthase, characteristic of the 2nd group, and are only to some extent associated with sex.With homozygous insufficiency of the enzyme cystatinin-3 synthase, there is a violation of the conversion of homocysteine to cystine, which is typical in Marfan's syndrome.

We have studied the markers of bone formation and bone resorption, that is, ALP and osteocalcin in CTD in age groups; at the age of 10-13 years osteocalcin -19.54±2.54 ng/ml; ALP -71.3±4.21 units/l; at 14-18 years old -16.24±1.28; -65.35±2.88.Comparative assessment of the average values of ALP and osteocalcin, obtained as a result of a random sample in patients aged 10-13 years and 14-18 years old with CTD, did not reveal significant deviations of bone formation markers from the allowable physiological fluctuations of these indicators (p <0.05).However, a more differentiated approach to the analytical assessment of bone formation markers, taking into account the genetic determinant, showed that in UDCTD (n=33) and DCTD (n=59) there are highly quantitative differences in the content of ALP and osteocalcin in the blood, not only in relation to these indicators in C/G, but also between the 1st and 2nd groups of the examined.

CONCLUSIONS

Thus, the state of hard tissues of teeth against the background of reduced BMD is characterized by a high intensity of carious lesions and their complications of hard tissues of teeth.Also, the revealed high correlation between the state of calcium homeostasis and the intensity of the carious process indicates the cause of secondary adentia in patients with reduced BMD of the skeleton - a violation of the mineralization of hard dental tissues.At the same time, in patients with CTD, there are changes in periodontal tissues that are characteristic of severe periodontal pathology.Low BMD of the skeleton may be associated with the level of bone resorption of the alveolar part of the jaws; the loss of alveolar bone in CGP is more pronounced, with systemic osteoporosis and osteopenia, the loss of bone tissue of the alveolar process is generalized, uniform in the area of all teeth, with the preservation of the shape of the interalveolar septa and the continuity of the cortical plate at the same time, on the OP of the jaws against the background of general porosity of the bone tissue stands out bone beams.

An imbalance in the system of calcium regulating hormones in middle-aged patients with DCTD and UDCTD of both sexes contributes to the development of an aggressive course of the disease, which is determined by a significantly significant (p<0.05) deterioration in all indicators of periodontal indices, an increase in attachment loss and a greater degree of bone tissue

resorption.The mechanism of bone resorption of the alveolar process in middle-aged patients with CTD pathologies is based on a violation of the bone remodeling cycle against the background of an imbalance of Ca regulating hormones, while a decrease in the rate of bone formation against the background of a normal level of bone resorption is the cause of the development of pathology of teeth and periodontal tissues.

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