



ORIGINAL ARTICLE

Research of connective tissue dysplasia influence on teething



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Abstract Purpose: This work aimed to study the rate and quality of maturation of the mineral component of retained teeth 3.8, 4.8 and lower jaw fragment of a human in connective tissue dysplasia in different periods of postpartum ontogenesis.

Methods: The study involved 102 men (76 with connective tissue dysplasia and 26 without connective tissue dysplasia) divided into groups by age: 31–40, 41–50, 51–60 years. One tooth 3.8, 4.8 and a fragment of the alveolar part of the lower jaw in the projection of teeth 3.8, 4.8 0.5*0.5 cm in size were extracted from each examinee for medical indications.

Results: Low optical density values are observed at the age of 41–50 years, at the age of 51–60 years, indicating decreased mineral density and the presence of total areas of hypomineralization from the age 31–40 years in connective tissue dysplasia. At the age of 41–50, 51–60 years, at the boundary of connective tissue structures and periosteum, a pronounced sclerosis and deformation of delineation elements were observed; at the age of 31–40 years, the indicated changes were less pronounced. At the age of 31–40 years, the level of bone plate dissection has a local character, after 40 years, it has a generalized character.

Conclusion: Progressive osteoporosis of the mandible and incomplete amelogenesis are an obstacle to the correct and harmonious teething of the lower wisdom teeth after the age of 30.

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1. Introduction

Connective tissue dysplasia is a large group of hereditary conditions leading to mutations in different genes and manifesting by different clinical phenotypes, eventually by human appearance, which has recently attracted the special attention of

doctors of different medical specialties (Kravtsov and Yavorskaya, 2017). In the case of connective tissue dysplasia (CTD), the rate of maturation of the mineral component of tooth enamel characteristics of bone tissue at a young age is reduced, which in turn is reflected in the quality parameters of enamel and bone tissue in later age, determining its rigidity, exposure to pathological conditions of the dentoalveolar apparatus (Vagner et al., 2019; Vagner et al., 2020a; Konev et al., 2018; Shen et al., 2020). These changes disrupt the normal process of development and teething of human teeth, preventing the coherence of the genetically determined complex of physical and chemical processes occurring in the enamel and bone tissue (Leontev, 2016; Koldehoff et al., 2020).

Undoubtedly, the above problems change the course, the nature of physiological and pathological processes in the maxillofacial region, which is determined by the general laws of nature and the evolutionary unity of the organism, eventually in connective tissue dysplasia, characterized by early acceleration changes (Kerrigan et al., 2019; Vagner et al., 2021). This leads to premature or late teething, which negatively affects the functional and aesthetic ability of the masticatory apparatus (Vagner et al., 2020b; Dean et al., 2020; Pandya and Diekwisch, 2019; Hogg and Richardson, 2019; Carreon and Funkenbusch, 2019). Because of the above, it is possible to question the known theories of teething, which reflect the course of the above processes in physiological conditions (Badruddin et al., 2020).

The work aims are to study the rate and quality of maturation of the mineral component of retained teeth 3.8, 4.8, and lower jaw fragment of a human in connective tissue dysplasia in different periods of postpartum ontogenesis.

2. Materials and methods

The study group consisted of 76 male patients with connective tissue dysplasia, 26 patients without connective tissue dysplasia (comparison group) who applied to the general dentistry department of Omsk region "City clinical dental polyclinic No.1" concerning the removal of retained tooth 3.8 or 4.8 for orthodontic or prosthetic indications. Comprehensive assessment of CTD definition was carried out using diagnostic tables and coefficients, calculated using Kulbak criteria. Skeletal phenotypic features (asthenic type of constitution, dolichomyelia, arachnodactelia, tower skull, hypertelorism, sandal cleft, vagus or valgus deformity of legs) were determined in all examinees, great attention was paid to the detection of dental stigmas (micro dentition, shovel teeth, tremas, diastemas, bite disorders, short bridles). All examinees were divided into 3 age subgroups: 31–40, 41–50, and 51–60 years of age. To study the inorganic component of tooth enamel authors carried out a densitometric assessment of its optical density using the computer tomography program Kodak Dental Systems (Trophy 2000).

A simple linear regression line was calculated by binary regression using the equation (Eq.1):

$$y = \alpha + \beta x, \quad (1)$$

where y is the value expected for y if the value of x is known; it is called the predicted value of y ; x is called the independent, predictor, or explanatory variable; α is the free term (interception) of the estimate line; it is the value of y when $x = 0$; β is

the angle coefficient or gradient of the estimate line; it represents the amount by which y increases on average if x increases by one.

Preparation of grinds of teeth samples 3.8, 4.8 for atomic force microscopy (AFM) and electron microscopy was carried out by dosed grinding and polishing of enamel to purity class 14, under control of depth of ground tooth enamel tissues with a dental depth gauge, distinguished by precise measurements to 1 mm. After mechanical processing of the thin sections, the preparation was cooled with distilled water, dried using a propane burner at 36 °C, etched with 37% orthophosphoric acid with a final washing under a stream of distilled water. For histological examination, a fragment of the alveolar part of the mandible was fixed in 10% formalin and 5% trichloroacetic acid solution.

After decalcification, the mandibular fragment was washed with final neutralization of residual acid. Paraffin sections prepared according to the standard technique were stained with hematoxylin-eosin. The tooth enamel ultrastructure was examined using a Solver Pro scanning probe microscope (NT-MPT, Russia). Computer processing of AFM-image samples was performed using Image Analysis NT-VDT software. As a result, the shape, surface, packing density, and distance between enamel prisms of teeth 3.8 or 4.8 was analyzed. The obtained data were processed by methods of variation statistics using standard packages Microsoft Excel 2008, Statistica 12.0.

3. Results and discussion

By the present time, the presence of age dimorphism of human teeth has been proved. Objective assessment of morphometric and morphological parameters of teeth is necessary in a comprehensive study of age-related variability of the maxillary apparatus, as well as reduction processes that occur differently in different age periods. In observations, the root system in the groups with and without CTD differs in low variability at ages 31–40, 41–50, 51–60 ($r_s = 0.281$, $p = 0.083$), the number of roots does not exceed two (31–40 years – 70%; 41–50 years – 80%; 51–60 years – 70%), no root fusion at these ages is observed. In the group with CTD at 31–40 years old, there were single observations of 3-rooted (<2%) and 4-rooted teeth (<2%) with tortuous abnormal structure, curvatures, but authors found no correlation in the studied indices ($r_s = 0.154$, $p = 1.014$). Morphometric parameters of the root system reflect the sufficient level of development and formation of the studied teeth (Table 1).

The optical density of the mineral component of the enamel of the studied teeth according to computed tomography (CT) densitometry increases with age in two groups (according to e1b: 31–40 years: $r_s = 0.485$, $p = 0.034$; 41–50 years: $r_s = 0.497$, $p = 0.032$; 51–60 years: $r_s = 0.638$, $p = 0.027$; for e2d: 31–40 years: $r_s = 0.689$, $p = 0.024$; 41–50 years: $r_s = 0.682$, $p = 0.025$; 51–60 years: $r_s = 0.522$, $p = 0.036$). In CTD, its values were high at age 31–40 years ($U = 2.0602$, $p = 0.0476$ relative to the 41–50 years group), at age 51–60 years ($U = 3.6029$, $p = 0.0239$ relative to the 41–50 years group), at age 41–50 years values were decreased ($U = 1.0628$, $p = 0.05291$). In the group without CTD, mineral density shows high values without at age 41–50 years ($U = 2.0388$; $p = 0.0315$ relative to group 31–40 years), at age 51–60 years ($U = 3.6029$, $p = 0.0239$ relative to group

Table 1 Macroscopic structure of the root part of teeth 38, 48 in different periods of postpartum ontogenesis.

Age group/Indicator	31–40 years with CTD/without CTD	41–50 years with CTD/without CTD	51–60 years with CTD/without CTD
Number of roots	1.7 ± 0.2/1.9 ± 0.2	1.6 ± 0.3/1.5 ± 0.2	1.8 ± 0.2/1.9 ± 0.3
Root length, mm	10.9 ± 1.3/10.7 ± 1.1	10.8 ± 0.8/10.9 ± 1.1	10.6 ± 0.5/10.7 ± 0.6

31–40 years). Age-related CT densitometric density values indicate a high level of maturity of the examined teeth in the group without CTD, with CTD the level of mineral density is reduced ($p < 0.05$). Analysis of CT densitometry and “curve” histograms in 95% of cases with CTD revealed a decrease in optical density of bone tissue. Despite an increase in optical density at age 31–40 years in CTD at points m1v1 ($r_s = 0.954, p = 0.047$) and m2al ($r_s = 0.871, p = 0.035$), after 40 years there is a decrease in mineral density, where total areas of hypomineralization appear. In both groups, the mandibular inclination angle in the area of teeth 3.8, 4.8 is more than 900, but in the group with CTD it is close to straight (at age 31–40 years $U = 5.959, p = 0.0092$ between group with and without CTD; at age 41–50 years $U = 4.5187, p = 0.0168$ between group with and without CTD), after 40 years a blunter inclination angle (Table 2).

No significant differences were obtained in the 51–60 years group (p greater than 0.05). The anatomical peculiarity of the lower jaw in the group with CTD has no negative impact on the process of teething of the studied teeth 3.8, 4.8. At 31–40, 41–50 years without CTD, the presence of roughness and irregularity on the enamel prisms was not observed, at similar ages with CTD, roughness and irregularity were minimal (Fig. 1 a, b; 2 a, b). At 51–60 years of age, the relief of the enamel prisms was completely absent in both groups. In both groups under study, authors did not detect branching into multiple prisms and their merging (Fig. 1 c; Fig. 2c).

The maximum peak of the mineral component occurred at 31–40 years of age; in the group without CTD, the maximum peak occurred at 51–60 years of age. Human tooth enamel in both groups contains large enamel prisms. In the group with CTD, small enamel prisms of ugly shape and configuration

are more common. In the group without CTD, small prisms are practically not visualized in the field of view of the atomic force microscope. In the group with CTD, there is a large amount of organic matrix and large distances between enamel prisms; in the group without CTD, the prisms are more densely packed. The magnitude of the distance between the enamel prisms decreases with age, in the group with CTD up to 40 years, without CTD up to 30 years, thereafter does not change. At ages 31–40, 41–50, 51–60, authors observed the presence of prismatic envelope in the form of a barely noticeable rim interrupted in some areas of enamel prisms in the group without CTD (Table 3).

At the histological examination of bone tissue at the ages of 41–50, 51–60 there is pronounced sclerosis and deformation of delineation elements at the border of connective tissue structures and periosteum, at the age of 31–40 these changes are expressed moderately, in the periosteum proper and compact layer of mandible there are changes of bone element structures: at age 31–40 years the haversian canals are dilated, in which pronounced tortuosity and multiplication of vessels are observed, at the ages of 41–50, 51–60 the haversian canals are narrowed, tortuosity and multiplication of vessels are less pronounced (Table 4).

In some areas in the bone tissue itself in all the examined patients, there is a predominance of osteoblasts and pronounced vacuolization of osteocytes. The mentioned changes testify to the balance of destructive and regenerative processes of bone tissue in the projection of un-cut teeth 3.8, 4.8. The study of the compact and cancellous substance of the mandible shows that gradual changes in the bone structure begin, which is associated with dystrophic degeneration of the bone structure of the compact and cancellous substance, with focal thin-

Table 2 Analysis of the densitometric density of the enamel mineral component of the teeth 38, 48 and the mandibular bone in different periods of postpartum ontogenesis.

Points for measuring the optical density of the mandibular hard tissues (M ± m)	31–40 years with CTD/without CTD	41–50 years with CTD/without CTD	51–60 years with CTD/without CTD
e1b of tooth enamel (units)	827.39 ± 20.21*/ 655.11 ± 21.38**	884.37 ± 24.23*/ 611.37 ± 18.83**	908.12 ± 25.11*/ 801.48 ± 22.34**
e2d of tooth enamel (units)	879.97 ± 22.14*/ 698.52 ± 25.59**	902.44 ± 17.26*/ 632.13 ± 19.25**	964.57 ± 23.17*/ 804.52 ± 23.08**
m1v1 of mandibular (units)	478.32 ± 18.77*/ 404.98 ± 24.21**	445.67 ± 21.51*/ 395.33 ± 25.56**	419.82 ± 23.18*/ 370.15 ± 24.89**
m2al of mandibular (units)	532.65 ± 15.87*/ 460.47 ± 25.92**	498.69 ± 18.11/447.6 ± 25.31**	491.14 ± 19.88/ 424.58 ± 26.72**
Ams (°)	138.51 + 3.3/99.23 + 3.8**	139.92 + 3.8/110.45 + 5.7**	143.47 + 3.7/115.69 + 4.9**
Amd (°)	137.13 + 3.1/102.34 + 3.6**	137.78 + 3.5/127.41 + 3.7**	145.98 + 4.2/132.56 + 4.1**

Note: statistical significance was calculated * – between age groups; ** – between groups with and without CTD ($p < 0.05$).

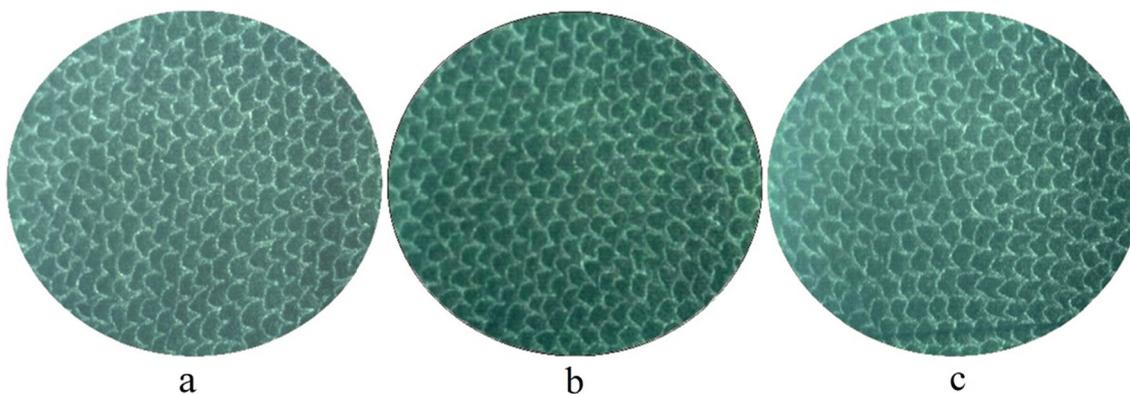


Fig. 1 Orientation of enamel prisms in the group without CTD in different periods of human postpartum ontogenesis (electron microscopy). P. $\times 1000$: a) at 31–40 years; b) at 41–50 years; c) at 51–60 years.

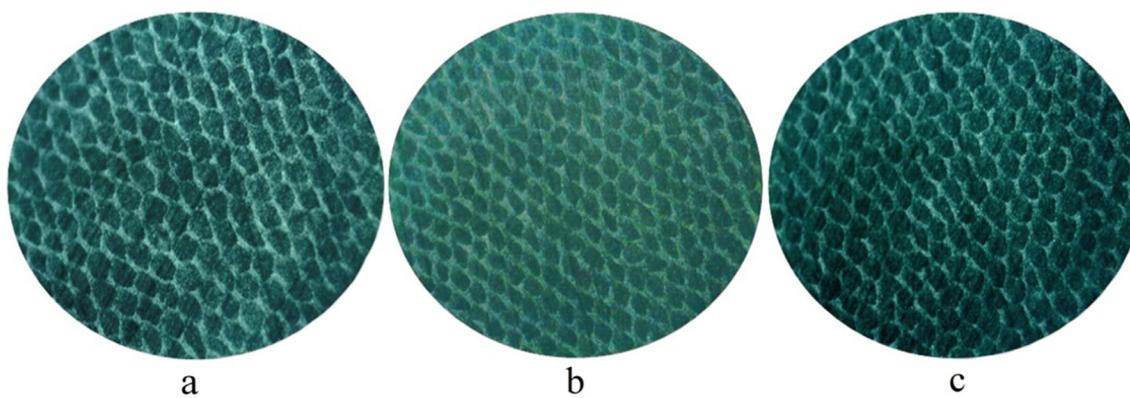


Fig. 2 Orientation of enamel prisms in the group with CTD in different periods of human postpartum ontogenesis (electron microscopy). P. $\times 1000$: a) at 31–40 years; b) at 41–50 years; c) at 51–60 years.

Table 3 Dimensional parameters of the mineral component and organic matrix of teeth enamel 38, 48 in different periods of postpartum ontogenesis.

Indicators	31–40 years with CTD/without CTD	41–50 years with CTD/without CTD	51–60 years with CTD/without CTD
Length of enamel prisms, nm	$5.58 \pm 0.22^*/4.26 \pm 0.24^{**}$	$6.01 \pm 0.26/3.82 \pm 0.21$	$6.23 \pm 0.14/3.96 \pm 0.27$
Width of enamel prisms, nm	$4.76 \pm 0.25^*/4.01 \pm 0.21^{**}$	$5.12 \pm 0.11/3.12 \pm 0.18^{**}$	$5.21 \pm 0.27/5.28 \pm 0.24$
Distance between enamel prisms, nm	$0.53 \pm 0.03^*/3.24 \pm 0.46$	$0.37 \pm 0.04/3.33 \pm 0.12$	$0.32 \pm 0.01/3.55 \pm 0.22$
Prismatic shell size, nm	менее 1.0/менее 1.0	менее 1.0/менее 1.0	менее 1.0/менее 1.0
Size of the inter-prism gap, nm	$2.09 \pm 0.28/3.05 \pm 0.52$	$2.06 \pm 0.21/3.14 \pm 0.47$	$1.98 \pm 0.17/2.74 \pm 0.65$

Note: statistical significance was calculated * – between age groups; ** – between groups with and without CTD ($p < 0.05$).

Table 4 Age-related changes in morphometric parameters of the lower jaw in the group with connective tissue dysplasia ($M \pm m$, P).

Morphometric indicators/Age	31–40 years	41–50 years	51–60 years
Volume density of compact matter (cortical layer, in relative units)	$35.22 \pm 3.1^*$	$28.12 \pm 3.9^*$	$26.53 \pm 2.3^*$
Volume density of cancellous bone (r.u.)	$39.98 \pm 6.9^*$	34.57 ± 5.5	$30.91 \pm 3.67^*$
Index of the ratio of spongy matter to compact matter	1.13 ± 0.2	1.1 ± 0.1	1.08 ± 0.2
Average number of haversacks in the field of view	$4.5 \pm 0.2^*$	3.8 ± 0.1	3.7 ± 0.2
Average number of vessels in the field of view	$16.02 \pm 2.01^*$	$14.23 \pm 1.57^*$	$12.57 \pm 2.1^*$
Average diameter of the haversacks	3.6 ± 0.3	3.51 ± 0.2	3.44 ± 0.3

Note: statistical significance was calculated * – between age groups ($p < 0.05$).

ning at age 31–40 years, and total thinning at age 41–50 and 51–60 years, saponification of compact plates is observed at all ages. With the progression of osteoporosis, numerous large ossicular spaces arise, which are vividly present at age 51–60 years. With increasing age, the bone plates become similar in structure to the spongy substance (Table 4).

According to the results of the given research, authors established that in the case of connective tissue dysplasia, the process of teething 3.8, 4.8 is suspended in conditions of low hypomineralization of dental hard tissue and pronounced hypomineralization of the mineral component of the mandible, despite the favorable anatomical conditions in the form of change of the mandibular inclination angle towards its obtuseness. After 30 years of age, the presence of irregularities and roughnesses on the surface of enamel prisms is found in minimal amounts, enamel prisms have a sufficient level of packing, in insignificant amounts ugly and irregularly shaped enamel prisms are traced, which indicates the presence of local areas of hypomineralization (Vatlin, 2006; Subramani and Mehta, 2018). After 40 years of age, in the connective tissue structures and periosteum of the lower jaw in the projection of retained teeth 3.8, 4.8 authors observe pronounced sclerosis and deformation of delineation elements, at the age of 31–40 these changes are of moderate character.

4. Conclusions

The study showed that morphometric parameters of the crown and root systems of teeth 3.8, 4.8 indicate the sufficient level of their formation. Atomic force microscopy study of mineral component ultrastructure of teeth and lower jaw enamel indicates marked age-related dimorphism of their structure, in the lower jaw – progressing sclerotic and degenerative changes, with deformation and splitting of bone plates at the majority fibrils level, typical for osteoporosis. The studied changes in connective tissue dysplasia in teeth 3.8, 4.8, and bone tissue are characterized by the insufficient rate of maturation of dense tissues of the maxillofacial region, by the presence of hypo mineralized areas. Unfavorable morphofunctional conditions decrease the probability of teething of teeth 3.8, 4.8 after the age of 30.

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None.

Ethical approval

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of: Ethics Committee of Federal State Budgetary Educational Institution of Higher Education “Omsk State Medical University” of the Healthcare Ministry of the Russian Federation. The approval code for this study is: No. 113.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.sdentj.2022.05.002>.

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