Influence of Vitamin D3 Deficiency on the Development of Malocclusions

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Abstract

Background: Insufficient or excessive growth of the craniofacial bone leads to skeletal and dental defects, which in turn result in the presence of malocclusions. To date, all causes of malocclusion have not been fully explained. In the development of skeletal abnormalities, attention is often paid to general deficiencies - including vitamin D3 deficiency, which causes rickets in growing people. It is suspected that its chronic deficiency may also affect the development of skeletal malocclusion. The aim of the study was to prospectively assess the impact of vitamin D deficiency on the development of malocclusions.

Methods: The examination consisted of three parts - (1) medical interview, (2) orthodontic examination along with an alginate impression and radiological imaging, (3) taking a venous blood sample for vitamin D3 level testing.

Results: In about 42,1% patients the presence of a skeletal defect was found. In 46,5% of patients presence of dentoalveolar malocclusion occurred. The most common skeletal defect was jaw narrowing in turn, among malocclusions most often retrogenia was diagnosed.

Conclusions: A relatively small number of patients in the study group was diagnosed with skeletal malocclusion. Due to effects of vitamin D on the development and metabolism of bones, including jawbones, and the relationship with, for example, rickets, we believe that it would be worthwhile to conduct a study fully focused on the group of patients with skeletal defects.

Background

The growth and development of jawbones are influenced by various genetic and environmental factors, dysfunctions and parafunctions, such as thumb sucking and mouth breathing [1,2]. Insufficient or excessive growth of the craniofacial bone leads to skeletal and dental defects, which in turn result in the presence of malocclusions. According to the current classification Orlik-Grzybowska classification, malocclusion is assessed in the following planes: sagittal, frontal and horizontal [1] and divided into vertical, horizontal and transverse. Basically, there are skeletal, dental and mixed defects.

To date, all causes of malocclusion have not been fully explained. Moyers et al. distinguish six categories of malocclusions: hereditary, developmental of unknown origin, trauma, physical factors, habits and diseases [1, 3]. Karłowska, on the other hand, divides the causes of such abnormalities into general (heredity, endocrine disorders, systemic diseases, extrinsic factors, e.g. improper position of the fetus, mechanical pressure caused by e.g. tumor, avitaminosis, effects of drugs, etc.) and local (dysfunctions, parafunctions, caries, injuries, etc.) [1].

In the development of skeletal abnormalities, attention is often paid to general deficiencies - including vitamin D3 deficiency, which causes rickets in growing people. It is suspected that its chronic deficiency may also affect the development of skeletal malocclusion. This vitamin is produced endogenously in the body and provided in the diet (fatty fish, eggs, dairy products, nuts). Under the influence of UVB radiation,

it is synthesized in the skin. Its production by photolysis is influenced by environmental and geographic factors, e.g.: latitude, season, weather, the angle of incidence of the sun rays, cloud covering, clothing (the degree of covering the body with clothes), time spent in the sunlight [4]. This hormone exerts a pleiotropic effect, influencing the calcium-phosphate balance and the maintenance of bone function and metabolism [5,6]. Moreover, medicine proves its pleiotropic effect, and thus its influence not only on bone structures (being a risk factor of osteoporosis, osteomalacia, fractures) but also on the development of cardiovascular diseases, obesity, hypocalcemia, cancer, diabetes, depression, autoimmune diseases [7,8]. Chronic deficiency in children causes rickets, leading to skeletal abnormalities, short stature, delayed skeletal development [7]

The problem of deficiency of this vitamin is global, even in highly sunlit regions [9]. A blood concentration below 30ng/ml (75nmol/l) is considered as a deficiency [10].The role of vitamin D3 in oral and maxillofacial sciences is significantly less discussed. Its significant impact on oral health has been demonstrated, showing that its deficiency increases the risk of periodontitis, alveolar bone loss, periimplantitis, caries, oral cancer, and osteonecrosis due to bisphosphonate treatment [11,12,13]. However, its unequivocal influence on the development of malocclusions has not been assessed so far. It seems that its chronic deficiency could be a significant factor modulating the development of skeletal defects in children, especially such as narrowing and shortening of the arches, maxillary and mandibular narrowing, micrognathia, microgenia, retrogenia. Malocclusions are often complex, so usually, the disorder occurs in several planes, and not as an isolated defect.

For example, a narrow maxilla with a narrow upper dental arch in relation to the width of the face, a high arched palate, a crossbite, a palatal tilt of the upper teeth, as well as crowdings are the causes of difficult functioning. The common dark cheek tunnels and crowding in the upper arch negatively affect the aesthetic aspect. Importantly, patients also complain of the need to breathe with their mouths due to obstruction of the upper respiratory tract, allergies, frequent colds, and tonsil hypertrophy. Similarly, the shortening of the dental arch as a result of anteroposterior maxillary hypoplasia is characterized in clinical examination by a deep nasolabial fold, shortening of the dental arch, and crowding of teeth. In some cases, jawbone development is inhibited in all three dimensions, resulting in microgenia or micrognathia. Microgenia so-called "bird's profile" often accompanies Pierre Robin syndrome [1]. Micrognathia is accompanied by pseudo occlusion with a bilateral crossbite. It is often associated with clefts and genetic syndromes such as Crouzon and Apert syndrome. The morphological hindquarters result from the inhibition of the front growth of the mandible as well as other changes in its structure. The mandibular ramus is usually shortened. The chin is set back, often accompanied by the elongation of the lower part of the face. It is a developmental defect that intensifies as a result of past rickets [1]. These defects significantly negatively affect both the functional and aesthetic aspects and require specialized multidisciplinary treatment.

Materials And Methods

The aim of the study was to prospectively assess the impact of vitamin D deficiency on the development of malocclusions.

Research group

A prospective observational study was conducted in a randomly selected group of patients from a private dental practice in Wrocław between 2017-2018. The analysis included patients of both sexes, Caucasian above 15 years of age. The study excluded people currently undergoing oncology treatment, treated with bisphosphonates, denosumab and angiogenesis inhibitors, pregnant women, patients with severe gastrointestinal diseases with chronic diarrhea, after extensive resections in the gastrointestinal tract, especially in the small intestine. For patients who had undergone orthodontic treatment, the initial malocclusion was described as the patients had been treated in this dental practice from the beginning and we had access to all necessary clinical data (patient who have been included in this study have been orthodontically treated for maximum a year). All participants or their legal guardians were acquainted with the subject of the study and gave their informed consent to participate in the project.

Components of the research

The examination consisted of three parts - (1) medical interview, (2) orthodontic examination along with an alginate impression and radiological imaging, (3) taking a venous blood sample for vitamin D3 level testing.

The interview included: demographic data (age, sex, height, body weight), habits (smoking, alcohol consumption, diet, last summer vacation in the sunlight, vitamin D3 supplementation), accompanying systemic diseases, medications, past orthodontic treatment.

A detailed examination of the oral cavity assessed: canine and Angle's class [1] on both sides, if the first molar or canine was missing, the class on this side was not assessed, vertical and horizontal overbite (in millimeters), crowding on the three-point Hotz scale [1970] in the maxilla and the mandible: 1st degree - no space for half of the incisal tooth, 2nd degree - no space for one and a half incisors, 3rd degree - no space for 2 or more incisors. The second and third degrees indicate extraction treatment needs. Malocclusion (in the sagittal, horizontal, orbital plane according to Karłowska [2]) was also evaluated.

Each patient underwent an alginate impression to prepare a plaster diagnostic model for analysis, an intraoral radiograph showing the upper and lower incisors, and volumetric tomography of the maxillary and mandibular region using a Carestream® device (Carestream Health, New York, USA).

Laboratory tests of venous blood collected from the elbow fossa were also performed. The blood sample was collected in a special tube, stored in a refrigerator after collection, and then, every 2 hours, collectively transported vertically in a portable refrigerator to a certified Dialab laboratory in Wrocław. The study gave: concentration of vitamin 25 (OH) D metabolite - determined by the immunochemical method. Vitamin 1,25 (OH) 2 was determined at the Synlab laboratory in Warsaw using the EIA method (enzyme immunoassay).

The reference values were: Vitamin 25 (OH) D

Children: 15-19 years - 4.8-42.32 pg / ml

Adults: 20.0 ng / ml - deficit; 20-30 ng / ml - too low level; 30-50 ng / ml - optimal level; 50-100 ng / ml - the level is too high; ≥ 100 ng / ml - toxic level.

For quantitative variables, basic descriptive statistics were calculated: means (M), standard deviations (SD), medians (Me), lower (Q1) and upper (Q3) quartiles, and extreme values: the smallest (Min) and the largest (Max). The consistency of empirical distributions of quantitative continuous variables with the theoretical normal distribution was established using the Shapiro-Wilk test, and the homogeneity of variance using the Levene and Brown-Forsythe tests. Nominal qualitative and ordinal variables are presented in multi-way (cross) tables in the form of count (n) and proportion (%). The significance of differences in mean values of variables with a distribution close to the normal in the two groups was verified with the Student's t-test. If the empirical distribution in any of the groups differed from the normal, the non-parametric Mann-Whitney U test was used. In the case of a larger number of groups, the analysis of variance (ANOVA) or the Kruskal-Wallis test was used, respectively. The strength and direction of the relationship between the two quantitative variables was estimated by calculating the Pearson correlation coefficients r. Data were analyzed with Statistica v. 13 (StatSoft Inc, Tulsa, USA). Statistical significance for all statistical tests was set at $p < 0.05$.

Results

The analysis included 114 patients (53 men and 61 women) aged 15-62 years (mean 36.5 ± 11.8 years) who completed their medical interview, participated in the clinical examination and donated a blood sample for laboratory tests.

In the studied group of patients, the majority of people denied vitamin D3 supplementation (73.6% N = 84). Only nearly a quarter of all respondents declared taking this vitamin, while the patients took small doses (500-2000 IU per day) of vitamin D3 alone, without calcium and vitamin K2.

General information and habits

Exposure in the sunlight during the last six months were declared by 21.9% of patients. The profile of the examined people can be described as generally healthy, conscious people, with a relatively high quality of life, hence the accompanying systemic diseases did not exceed a dozen or so percent (autoimmune - 13.2%; gastrointestinal - 8.8%; cardiovascular - 4.4 %; metabolic - 0.9%). Proper hygienic habits, that is: using a toothbrush with an appropriate technique for more than 2 minutes at least twice a day and regular use of an irrigator or dental floss were found in 35.1% of respondents. 40 people (35.1%) had the habit of grinding their teeth. Tooth abfractions, attritions occurred in almost half of the cases (50.5%).

Skeletal and dentoalveolar status

In about 42,1% patients the presence of a skeletal defect was found. In 46,5% of patients presence of dentoalveolar malocclusion occurred .Most of the patients presented I Angle and canine class. The most common skeletal defect was jaw narrowing in turn, among malocclusions most often retrogenia was diagnosed. Moreover, 85 patients had crowdings - 50 in the lower jaw and 35 in the upper jaw. In addition, 28.1% had periodontal disease with the presence of pathological periodontal pockets, measured with the WHO 621 probe. In turn, class I recessions according to Miller was found in 22.8% of patients, second class in 15.8% of patients and third class in 17.5% of patients [Table 1].

feature	n (%)
bite assessment - right side	
● Angle I class	56 (49,1%)
● Angle II class	20 (17,5%)
● Angle III class	14 (12,3%)
● no assessment / not applicable	24 (21,1%)
bite assessment - right side	
● canine I class	76 (66,7%)
● canine II class	23 (20,2%)
● canine III class	8 (7,0%)
● no assessment / not applicable	7 (6,1%)
bite assessment - left side	
● Angle I class	53 (46,5%)
● Angle II class	20 (17,5%)
● Angle III class	17 (14,9%)
● no assessment / not applicable	24 (21,1%)
bite assessment - left side	
● canine I class	77 (67,5%)
● canine II class	23 (20,2%)
● canine III class	8 (7,0%)
● no assessment / not applicable	6 (5,3%)
malocclusions	
● distoclussion	10 (8,8%)
● retrogenia	18 (15,8%)
● mesioclussion	4 (3,5%)
● progenia	6 (5,3%)
● anterior open bite	5 (4,4%)
● lateral open bite	1 (0,9%)
● deep bite	23 (20,2%)
● tete-a-tete	10 (8,8%)

●	crossbite	20 (17,5%)
●	lingual crossbite	2 (1,8%)
●	narrow upper arch	35 (30,7%)
●	widened upper arch	3 (2,6%)
●	shortened upper arch	4 (3,5%)
●	spaced upper arch	14 (12,3%)
●	narrow lower arch	14 (12,3%)
●	widened lower arch	6 (5,3%)
●	shortened lower arch	3 (2,6%)
●	spaced lower arch	8 (7,0%)

Table 1. Skeletal and dentoalveolar features; N- number of patients.

Vitamin D serum level

The concentration of vitamin 25 (OH) D in the study group ranged from 7.8 to 57 [ng / ml], on average 23.6 ± 10.5 [ng / ml]. In accordance with the adopted refrain values, its deficiency was found in 86 subjects (75.4%) (level up to 30 ng / ml) [Table 2].

feature	supp. YES N=29		supp. NO=85		Y vs N (p)
vitamin D levels [ng/ml]:	n	%	n	%	
deficit (up to 30,0 ng/ml)	12	41,4%	74	87,1%	**<0,001**
optimal (above 30,0 mg/ml)	17	59,6%	11	12,9%	
vitamin D levels [ng/ml]:					
M ± SD	33,36 ± 11,89		20,25 ± 7,47		
Me [Q1; Q3]	33,0 [23,6; 39,9]		19,1 [15,2; 25,5]		**0,001**
Min - Max	11,5 - 57,0		7,8 - 41,9		

Table 2. Supplementation of vit.D

It was shown that in the group of patients with optimal and overstated vitamin D3 levels, the assessment of bite correctness analyzed together (Angle's class on the left and right) was significantly better than in patients with deficiency or undervalued D3 concentration ($p < 0.05$). The relationships between skeletal and dental malocclusion of canine classification, the difference in favor of patients with normal D3 concentration remained at the border of statistical significance ($p = 0.087$) [Table 3].

Overall risk factors for vitamin D deficiency have been defined [Table 3].

Risk factors	Vitamin D deficiency		test of independence	OR (95% PU)
	YES	NO		
	N=86	N=28		
age up to 28 years	**31 (36,0%)**	**4 (14,3%)**	**p=0,035**	**3,38 [1,05; 9,89]**
sex- men	**57 (66,3%)**	**4 (14,3%)**	**p<0,001**	**11,8 [3,74; 37,2]**
lack of vitamin D supplementation	**74 (86,0%)**	**10 (35,7%)**	**p<0,001**	**11,1 [4,07; 28,6]**
unfavorable factors	57 (66,3%)	17 (60,7%)	p=0,529	1,27 [0,53; 3,06]
holidays in the sunlight	18 (20,9%)	8 (28,6%)	p=0,388	0,66 [0,25; 1,71]
vegetarianism	3 (3,5%)	1 (3,6%)	p=1,000	0,98 [0,10; 7,00]
cardiovascular diseases	3 (3,5%)	2 (7,1%)	p=0,595	0,59 [0,08; 2,64]
gastrointestinal diseases	6 (7,0%)	4 (14,3%)	p=0,257	0,45 [0,12; 1,65]
autoimmune disorders	8 (9,3%)	7 (25,0%)	p=0,031	0,31 [0,10; 0,93]
metabolic disorders	0 (0%)	1 (3,6%)	p=0,246	-
proper hygienic habits	30 (34,9%)	10 (35,7%)	p=0,936	0,96 [0,40; 2,32]
teeth overloads	45 (52,3%)	13 (50,0%)	p=0,835	1,10 [0,46; 2,62]
CAL- clinical attachment loss	**52 (60,5%)**	**9 (32,1%)**	**p=0,010**	**3,23 [1,30; 7,77]**
pathological periodontal pockets	**29 (33,7%)**	**3 (10,7%)**	**p=0,028**	**4,24 [1,15; 13,7]**
past orthodontic treatment	28 (32,6%)	8 (28,6%)	p=0,693	1,21 [0,52; 2,84]
skeletal malocclusions	40 (46,5%)	8 (30,8%)	p=0,142	2,00 [0,78; 4,96]
crowdings	41 (47,7%)	12 (42,9%)	p=0,657	1,21 [0,52; 2,84]
bruxism	31 (36,1%)	9 (32,1%)	p=0,707	1,19 [0,48; 2,89]

Table 3. Comparison of qualitative characteristics of patients differing in vitamin D3 levels and test results.

In the group of patients up to 28 years of age, vitamin D deficiency was more frequent. The deficit was more common in men. People with a deficiency of vitamin D more often did not supplement vitamin D3. Vitamin D3 deficiency was more common in people with loss of connective tissue attachment and pathological periodontal pockets. Some trends are also observed, which, due to the relatively small group of respondents, lead to certain conclusions, although not statistically significant: In people with vitamin D3 deficiency, tooth overload, skeletal defects, tooth crowding and bruxism were more often observed.

Risk factors	Vitamin D deficiency		OR	OR (95% PU)	
	YES N=86	NO N=28		from	up to
skeletal malocclusions	28 (32,6%)	6 (21,4%)	1,71	0,59	4,94
crowdings	41 (47,7%)	12 (42,9%)	1,00	0,36	2,75
past orthodontic treatment	28 (32,6%)	8 (28,6%)	1,75	0,62	4,94
bruxism	31 (36,1%)	9 (32,1%)	0,62	0,16	2,35
malocclusion in Angle class.	28 (32,6%)	6 (21,4%)	1,77	0,65	4,85
narrowed upper arch	**31 (36,0%)**	**3 (10,7%)**	**4,94**	**1,38**	**17,7**
widened upper arch	3 (3,5%)	0 (0,0%)	-	-	-
shortened upper arch	2 (2,3%)	2 (7,1%	0,32	0,05	2,30
spaced upper arch	13 (15,1%)	1 (3,6%)	4,81	0,60	38,5
narrowed lower arch	11 (12,8%)	3 (10,7%)	1,22	0,32	4,74
widened lower arch	6 (7,0%)	0 (0,0%)	-	-	-
shortened lower arch	1 (1,2%)	2 (7,1%)	0,15	0,01	1,76
spaced lower arch	5 (5,8%)	3 (10,7%)	0,51	0,11	2,31
crowdings- upper arch	**32 (37,2%)**	**3 (10,7%)**	**4,94**	**1,38**	**17,7**
crowdings- lower arch	39 (45,3%)	11 (39,3%)	1,28	0,54	3,06
crossbite	**18 (20,9%)**	**2 (7,1%)**	**6,16**	**1,32**	**28,8**
lingual crossbite	2 (2,3%)	0 (0,0%)	-	-	-
anterior open bite	3 (3,5%)	2 (7,1%)	0,47	0,07	2,97
lateral open bite	1 (1,2%)	0 (0,0%)	-	-	-
deep bite	19 (22,1%)	4 (14,3%)	1,70	0,53	5,51
mesiocclusion	4 (4,7%)	0 (0,0%)	-	-	-
progenia	5 (5,8%)	1 (3,6%)	1,67	0,19	14,9
tete-a-tete	9 (10,5%)	1 (3,6%)	3,16	0,38	26,1
distoclussion	7 (8,1%)	3 (10,7%)	0,74	0,18	3,07
retrogenia	15 (17,4%)	3 (10,7%)	1,76	0,47	6,60

Table 4. Comparison of qualitative characteristics of patients differing in vitamin D3 deficiency and the value of the uncorrected odds ratio (OR).

Based on the results in table 4 it was shown that vitamin D deficiency negatively influences the maxillary development. These patients have been shown to be at greater risk of narrowed upper arch (OR=4,94), crowdings in upper arch (OR=4,94) and crossbite (OR=6,16).

Discussion

The positive effect of vitamin D on bone health has been known for a long time. It is believed to be closer to the hormone than vitamin because it is produced endogenously, and its action is not only mediating calcium-phosphate homeostasis. Vitamin D3 deficiency is a global problem that affects both healthy people and those with comorbidities, regardless of latitude, age, gender, and race. Interestingly, 83% of newborns are born with vitamin D deficiency, with 25 (OH) D levels <50 nmol / l. It may indicate vitamin D deficiency already in pregnant women. Moreover, other authors believe that prenatal vitamin D status appears to affect postnatal mineral homeostasis and may influence growth. Postnatal vitamin D status is fundamental to mineral homeostasis and may affect subsequent bone mass. The effect of vitamin D3 levels on dento-gingival status has not yet been fully elucidated, and the number of scientific publications on this topic is limited.

Most of the available studies concern the assessment of the effect of vitamin D3 on gingivitis and periodontitis. A study by Krall et al on a group of 145 people over 65 years of age showed that supplementation with calcium and vitamin D3 reduces the risk of tooth loss in the elderly. Zahn et al. also noted a significant correlation between vitamin D deficiency and tooth loss. Moreover, it should be emphasized that in the non supplementing group we studied, bruxism was observed in 38.8% of patients, and in 54.1%, various types of teeth overload (attrition, abfractions). In this group, the mean value of vitamin D was found at the level of 20.25 ± 7.7 ng / ml (Min - Max: 15.2 ng / ml - 25.5 ng / ml), so there was a deficit in accordance with the adopted reference ranges. Research by Singleton et al. and Schroth et al. indicate that prenatal vitamin D levels may influence the primary dentition and the development of ECC (early childhood caries), so improving vitamin D status in pregnant women might affect ECC rates in their infants.

In orthodontics, vitamin D deficiency may affect the slower movement of teeth under the influence of orthodontic forces, which has been confirmed in several researches. Based on the studies on rats, the authors concluded that the use of calcitriol may promote the reconstruction of surrounding tissues after orthodontic treatment. It seems that the proper vitamin D3 levels during orthodontic treatment may affect more effective bone remodeling, especially in the elderly. However, in the studies of Tehranchi and colleagues in 34 patients treated orthodontically with the use of fixed appliances, it was not shown that levels of vitamin D3 were associated with external root resorption. Although no such correlation was found, the researchers stressed that research in this area should be expanded as there are few scientific reports on the subject.

Our research did not evaluate the influence of vitamin D levels on the course of orthodontic treatment. As it was a prospective-observational study, only vitamin D levels were associated with malocclusion or dental defects. Teeth crowding in both the upper and lower arch, as well as skeletal defects, were more often found with correlation of a low vitamin D concentration. Skeletal defects occurred in 48,1% of cases.Narrowing of the upper dental arch was found significantly more often in patients with vitamin D deficiency. Crowdings occurred in 47.7% of cases. Moreover, 32.6% of patients with vitamin D deficiency presented for orthodontic treatment, which was a much larger group than the number of non-deficit patients. It was also observed in the study that Angle's class I, i.e. in the absence of a skeletal defect, was mainly accompanied by an optimal or excessive level of this hormone. It may result from this that the proper concentration of vitamin D3 in the body promotes the proper development of the bones of the face.

A relatively small number of patients in the study group was diagnosed with skeletal malocclusion. Due to the previously mentioned effect of this hormone on the development and metabolism of bones, including jawbones, and the relationship with, for example, rickets, we believe that it would be worthwhile to conduct a study fully focused on the group of patients with skeletal defects. Determination of baseline vitamin D levels and genetic studies of vitamin D receptor (VDR) polymorphisms could be helpful in determining prenatal and postnatal supplementation. It is very important, as increased skeletal defects result in functional disorders, chewing and breathing disorders, but also have a negative aesthetic aspect, and often also psychological and social ones. Their treatment is demanding, multidisciplinary, involving extensive surgical procedures.

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The research has been performed in accordance with the Declaration of Helsinki and has been approved by ethics committee - Wrocław Medical Univeristy (KB-442/2017) in year 2017. The research has been performed in accordance with relevant guidelines and regulations.

All participants or their legal quardians were acquainted with the subject of the study and gave their informed consent to participate in the project.

CONSENT FOR PUBLICATIONS

All authors and persons participating in the study consent to the publication.

AVAILABILITY OF DATA MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare they have no competing intrests

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AUTHOR'S CONTRIBUTION

MD design of the work

AL acquisition and analysis

SH draft and revision

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