

ОРТОДОНТІЯ

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THE STATE OF BONE METABOLISM IN PATIENTS WITH GENERALIZED PERIODONTITIS IN DIABETIC OSTEOPATHY

Diagnosis of the state of bone metabolism in patients with generalized periodontitis burdened with type 2 diabetes is an important step in the complex of treatment and prevention measures for this pathology. **The purpose of the study** was to create evidence-diagnostic criteria for assessing and predicting the severity of the course of generalized periodontitis in diabetic osteopathy based on the study of the variability of bone remodeling. **Research material and methods.** In order to select homogeneous groups, a clinical and radiological examination of 166 patients with generalized periodontitis, associated and not associated with type 2 diabetes, was conducted. The age of the patients was in the range of 30-50 years (on average 42.5±2.34 years). Among them there were 99 (59.6 %) women and 67 (40.4 %) men. The degree of severity of generalized periodontitis was verified according to generally accepted clinical and radiological criteria outlined in modern and domestic classifications: 76 (45.8 %) patients had chronic generalized periodontitis and 90 (54.2 %) had chronic rapidly progressive periodontitis. The control group consisted of 19 almost healthy voluntary donors of similar age (on average 41.5±2.7 years) and sex without endocrine pathology, with healthy periodontium and intact teeth. **Research results and their discussion.** Evaluation of the Hounsfield index and markers of bone metabolism in different groups of patients with generalized periodontitis in type 2 diabetes with average statistical analysis showed that they are directly correlated with the severity and the course of generalized periodontitis, the stage of compensation, the severity and duration of diabetes.

Conclusions. The peculiarity of the clinical course of generalized periodontitis in type 2 diabetes mellitus, burdened by diabetic osteoporosis, is caused and manifested by a decrease in the bone structures of the periodontium in the processes of osteosynthesis and an increase in the intensity of bone resorption. A feature

of the manifestation of rapidly progressive and chronic generalized periodontitis in diabetic osteopathy and without systemic pathology is the increase, independent of the clinical picture of the disease, of signs of osteoporosis activation and a decrease in osteosynthesis. To verify the activity of osteosynthesis and bone resorption in periodontal tissues, the following have predictive value: diagnosis of different directionality and intensity of bone remodeling based on the levels of quantitative content in blood serum of the levels of markers of bone metabolism. **Key words:** periodontitis, periodontal pathology, rapidly progressive generalized periodontitis, diabetes, markers of bone metabolism.

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СТАН КІСТКОВОГО МЕТАБОЛІЗМУ У ХВОРИХ НА ГЕНЕРАЛІЗОВАНИЙ ПАРОДОНТИТ ПРИ ДІАБЕТИЧНІЙ ОСТЕОПАТІЇ

Діагностика стану кісткового метаболізму у хворих на генералізований пародонтит, обтяженого цукровим діабетом 2 типу є важливим етапом у комплексі лікувально-профілактичних заходів при даній патології. **Мета** дослідження. Створення доказово-діагностичних критеріїв для оцінки і прогнозування тяжкості перебігу хвороби генералізованого пародонтиту при діабетичній остеопатії на основі вивчення варіабельності кісткового ремоделювання. **Матеріал і методи дослідження.** З метою відбору однорідних груп було проведено клініко-рентгенологічне дослідження 166 хворих на генералізований пародонтит, асоційованих та не асоційованих із цукровим діабетом 2 типу. Вік пацієнтів був у діапазоні від 30-50 років (у середньому 42,5±2,34 року). Серед них було 99 (59,6 %) жінок і 67 (40,4 %) чоловіків. Ступінь тяжкості генералізованого пародонтиту був верифікований згідно із загальноприйнятими клініко-рентгенологічними критеріями, викладеними в сучасних та вітчизняних класифікаціях: у 76 (45,8 %) хворих виявлений хронічний генералізований пародонтит та у 90 (54,2 %) хронічний швидкопрогресуючий пародонтит. Контрольну групу склали 19 майже здорових добровільних донорів аналогічного віку (у середньому 41,5±

2,7 років) і статі без ендокринної патології, зі здоровим пародонтом і інтактними зубами. **Результати дослідження та їх обговорення.** Оцінка показників індексу хаунсфілда та маркерів кісткового метаболізму у різних груп хворих на генералізований пародонтит при цукровому діабеті 2 типу при середньостатистичному опрацюванні продемонструвала, що вони перебувають у прямій кореляційній залежності від тяжкості й перебігу генералізованого пародонтита, стадії компенсації, тяжкості та тривалості цукрового діабету. **Висновки.** Особливість клінічного перебігу генералізованого пародонтиту при цукровому діабеті 2 типу, обтяженого діабетичним остеопорозом, обумовлена і проявляється зниженням в кісткових структурах пародонту процесів остеосинтезу і підвищенням інтенсивності остеорезорбції. Особливістю прояву швидкопрогресуючого і хронічного генералізованого пародонтиту при діабетичній остеопатії і без системної патології є наростання, незалежних від клінічної картини захворювання, ознак активації остеопорозу та зниження остеосинтезу. Для верифікації активності остеосинтезу і остеорезорбції в пародонтальних тканинах, предиктивну цінність мають: діагностика різної направленості і інтенсивності кісткового ремоделювання за рівнями кількісного вмісту в сироватці крові рівнів маркерів кісткового метаболізму.

Ключові слова: пародонтит, патологія пародонта, швидкопрогресуючий генералізований пародонтит, цукровий діабет, маркери кісткового метаболізму.

In recent years, there has been a steady trend towards the growth of bone pathologies among patients with type 2 diabetes. A high level of periodontal tissue morbidity is noted [1, 2, 3, 4] in this contingent of patients, the frequency of severe forms of generalized periodontitis is increasing [5, 6, 7, 13, 14]. The relationship between diabetes and periodontal diseases is confirmed by numerous studies by the authors [3, 6, 7, 9].

At the same time, a two-way relationship between periodontitis and diabetes is described [7, 8, 9]. It is noted that in patients with diabetes, inflammatory processes in the periodontium are more pronounced than in patients without this endocrine pathology, while the maximum level of inflammation was recorded in patients with uncontrolled diabetes [10, 11, 12].

In addition, it should be noted that diabetes is accompanied by various metabolic disorders, including bone metabolism. This explains the tendency of patients with this disease to osteopenia, osteoporosis and its activation in bone structures of the body as a whole and in periodontal tissues in particular.

Therefore, in the case of generalized periodontitis associated with diabetic osteopathy, clinical and laboratory studies demonstrating the interaction between markers of the state of bone metabolism and the clinical course of the pathological process in periodontal

tissues are of interest. The acquired knowledge will undoubtedly be useful both when choosing treatment tactics for generalized periodontitis and when planning preventive measures. Our research was aimed at solving this issue.

The aim of the study. Creation of evidence-diagnostic criteria for assessing and predicting the severity of the course of the disease of generalized periodontitis in diabetic osteopathy based on the study of the variability of bone remodeling.

Research materials and methods. In order to select homogeneous groups, a clinical and radiological examination of 166 patients with generalized periodontitis, associated and not associated with type 2 diabetes, was conducted. The age of the patients was in the range of 30-50 years (on average 42.5±2.34 years). Among them there were 99 (59.6 %) women and 67 (40.4 %) men.

In diagnosing the severity of diabetes, we focused on the clinical and laboratory data presented by our endocrinologists: patients with subcompensated and compensated forms of the disease were included in the study.

The degree of severity of generalized periodontitis was verified according to generally accepted clinical and radiological criteria outlined in modern and domestic classifications: 76 (45.8 %) patients had chronic generalized periodontitis and 90 (54.2 %) had chronic rapidly progressive periodontitis.

The control group consisted of 19 almost healthy voluntary donors of similar age (on average 41.5±2.7 years) and sex without endocrine pathology, with healthy periodontium and intact teeth.

The generally accepted clinical examination included the collection of complaints, anamnestic information, determination of the objective state of periodontal tissues using periodontal indices and instrumental methods.

The oral hygiene index was studied according to the method of Green, V. C. Vermillion (1964), the intensity and prevalence of the inflammatory process in the periodontal tissues was determined by the degree of bleeding from the dento-gingival groove (Muhlemann H. Cowell, 1975) and with the help of the papillary-marginal alveolar index (PMA), modified by C. Parma in 1960. The periodontal index (PI) according to Russel (1956) was used to objectify the severity and prevalence of inflammatory-destructive changes in periodontal tissues.

The "FLORIDA PROBE" system was used for simultaneous fixation of the depth of periodontal pockets, the presence of bleeding, dental deposits, and tooth mobility.

The degree of the destructive process in the periodontal tissues was assessed by orthopantomogram and cone-beam computed tomography (CBT) data obtained on a Planmeca Pro Max computed tomography scanner (Finland).

Changes in alveolar bone density in Hounsfield units were also determined using dental computed tomography. Value <300 units. considered as the presence of an active osteoporotic process in the bone tissue of alveolar sprouts.

Patients were included in the study only after signing the informed consent and familiarizing them with the objectives of the intended clinical and laboratory studies. The study did not include patients with other (except type 2 diabetes) risk factors for the development of secondary osteoporosis – thyrotoxicosis, chronic renal failure, bronchial asthma, treatment with thyroid hormones, and others.

The material for laboratory tests was blood serum, which was collected between 8 and 10 in the morning from the cubital vein on an empty stomach. All researched laboratory indicators on the same equipment, methodology and calculations did not change.

The state of bone remodeling – the intensity of the processes of resorption and formation of bone tissue was determined by the quantitative content of markers of osteosynthesis and bone resorption in blood serum. As markers of bone formation, the activity level of the isoenzyme of the bone fraction alkaline phosphatase (BAP) and BGLAP were chosen. The expression of the resorptive process in the bone tissue of alveolar sprouts was determined by the concentration level of tartrate-resistant acid phosphatase (TRACP) and C-terminal telopeptide of collagen type 1 breakdown – β -Cross-Laps. A complex and dynamic study of selected markers made it possible to study the peculiarities of the metabolic processes of systemic bone remodeling.

Mathematical data processing was carried out on a personal computer using the "STATISTICA" 99 software package (Version: 6.1 "Stat. Soft Inc.").

Research results. As a result of the evaluation of computer tomograms, signs of increased X-ray trans-

parency of the bone tissue of the alveolar sprouts were found, as a manifestation of active osteoporosis: in 56 (100%) chronic rapidly progressing generalized periodontitis (main group I),

The first comparison group (34) consisted of patients with a similar diagnosis, but without endocrine pathology and associated osteopathy. The indicators of the Hounsfield index were, respectively: 547 ± 10.8 versus 698.4 ± 15.6 . Among patients with chronic generalized periodontitis that occurred against the background of diabetes (II main group – 40 patients), only 5 (12.5 %) patients did not have X-ray signs of osteoporosis; according to the evaluation data of Hounsfield index, a reliable value of the decrease in the density of alveolar bone structures was established, but it is somewhat less than that level in patients with manifestations of rapidly progressing periodontitis on the background of diabetic osteopathy (616.2 ± 15.2 units of HU versus 547 ± 10.8 units of HU).

While, according to measurements of the bone tissue density of alveolar sprouts in patients with generalized periodontitis not associated with diabetic osteopathy (II comparison group – 36 patients), the Hounsfield index according to CPCT data was on average 783.2 ± 14.2 units of HU (at physiological norm 1032.6 ± 17.3 units HU), which indicated the absence of active osteoporosis in the bone structures of the periodontium (Table 1).

As can be seen from Table 2, the most significant decrease in the mineral density of bone structures of alveolar sprouts was found in patients with rapidly progressive generalized periodontitis occurring against the background of diabetic osteopathy (group I), the least in patients with chronic generalized periodontitis who did not have systemic diabetic osteoporosis, with therefore, in patients with rapidly progressive generalized periodontitis without endocrine pathology, the indicators of markers of the resorptive process were less moderate than in representatives of the I and II main groups.

The established fact of a sharp decrease in the density of bone tissue of alveolar sprouts with pro-

Table 1

Indicators of the Hounsfield index (HU units) in patients of the main group and the comparison group

Bone density indicators	Groups of examinees				
	I main group (n=56)	II main group (n=40)	I comparison group (n=34)	II comparison group (n=36)	control group (n=19)
Hounsfield index (in HU units)	$547 \pm 10,8^*$	$616,2 \pm 15,2^*$	$698,4 \pm 15,6^*$	$783,2 \pm 14,2^*$	$1032,6 \pm 17,3^*$

Note: $*p < 0.05$ – the significance of differences with the data of the control group.

** $p < 0.05$ – reliability of differences with the data of the main group.

Table 2

Indicators of markers of bone metabolism in patients of different observation groups

indicators of markers of bone remodeling	Groups of examinees				
	control group (n=19)	I main group (n=56)	I comparison group (n=34)	II main group (n=40)	II comparison group (n=36)
TRACP (Unit/L)	3,7±0,3	8,7±0,3**	5,9±0,2**	6,8±0,2**	4,7±0,2
β-CL (ng/ml)	1,16±0,6	5,87±0,2**	3,3±0,2**	4,8±0,2**	2,1±0,2
BAP (Unit/L)	36,9±0,9	14,7±1,2**	20,4±0,3**	19,7±0,4**	29,4±0,9*
BGLAP (mg/ml)	19,5±0,4	10,2±0,3**	13,4±0,6**	12,8±0,3**	16,6±0,6**

nounced destructive pathology of the periodontium against the background of diabetes indirectly indicated the possible activation of the osteoporotic process in the periodontal tissues, as well as its diffuse expression.

From the standpoint of evidence-based medicine, elucidation of the main mechanisms of activation of the osteoporotic process was carried out by means of a comparative analysis of the functional state of the bone in four groups of patients approximately equal in terms of gender, age, and severity of generalized periodontitis. Group I included patients with rapidly progressing generalized periodontitis occurring against the background of diabetic osteopathy (56 people); And the comparison group (34 people) consisted of patients with a similar diagnosis – rapidly progressing generalized periodontitis, not burdened by type 2 diabetes, without systemic osteoporosis; The II main group (40 people) was formed from patients with chronic generalized periodontitis against the background of type 2 diabetes with diabetic osteopathy; The II comparison group (36 people) was represented by similar patients without aggravating pathology and had questionable signs for assessing the type of osteoporotic process activity in the periodontal tissues.

Determination of the composition of markers of bone remodeling showed that the physiological level of tartrate-resistant acid phosphatase content in blood serum was significantly higher in individuals of group I compared to control numbers. An increase in TRACP levels was also recorded in patients of the II comparison group, although it was significantly less than in the group of patients with rapidly progressive generalized periodontitis, which occurred against the background of diabetic osteopathy (I group).

Minimal changes in the content of BAP were recorded in patients with chronic generalized periodontitis who did not suffer from systemic osteoporosis. In more than 4% of cases, the range of indicators was close to that of healthy people. It is worth noting that the reduction of BP in patients of the I and II groups was significant both with diabetic osteopathy

and without it. This indicates the possibility of a low manifestation of osteogenesis in the bone tissue of the periodontium in patients with rapidly progressive generalized periodontitis who do not suffer from concomitant type 2 diabetes mellitus, which is not burdened by systemic osteoporosis.

The results of determination of β-CL parameters in patients with chronic rapidly progressing periodontitis in diabetic osteopathy indicate an acceleration of the rate of bone degradation of alveolar sprouts. An increase in the β-CL index was established in 100 % of cases by more than 3.5 times the prevailing similar parameters of the control group (on average up to 4.02±0.2 mg/ml versus 1.16±0.3 mg/ml; p<0.05). Moreover, the more the bone mineral density of the alveolar bone is reduced, the higher the level of β-CL.

A pronounced increase in β-CL in the blood serum of patients of group I was associated with a pronounced activation of BAP in more than 80 % of patients (85.1 % of cases).

The presence of a close relationship mechanism between BAP resorption indicators and β-CL in patients of the I and II groups reveal the reliably significant informativeness of these indicators in the diagnosis of resorption activity in the bone, on the other hand, the level of β-CL changed more significantly in the representatives of the III group.

In the course of the study, it was found that the marker of bone resorption – β-CL has a high predictive value for identifying patients with different courses of generalized periodontitis.

The content of β-CL in the blood serum of patients with rapidly progressive generalized periodontitis, suffering from type 2 diabetes, burdened by systemic osteoporosis was high and was measured within the parameters of group I in 77.5 % of cases. At the same time, it should be noted that the levels of the analyzed marker of bone tissue resorption were moderate in other subjects. On average, its value in other groups was 3.4±0.2 mg/ml (norm 1.16±0.3 mg/ml). It is worth noting that the concentration of β-CL in the blood serum of patients of the I and II main groups, with active osteoporosis in the bone structures of the

periodontium established by computer diagnostics, was high in the majority of the examined (92.4 % of cases) and average was 5.3 ± 0.2 . Low numbers of β -CL in patients of the II comparison group once again demonstrate its predictive value for determining the active resorptive process.

The level of content of the main indicator of osteogenesis (bone formation) of serum BGLAP was significantly reduced only in patients I and II of the main study group (10.2 ± 0.3 and 12.8 ± 0.3 mg/ml) and indicated a significant and reliable inhibition of the processes bone formation Parameters of BGLAP concentration in patients with chronic generalized periodontitis, not burdened by type 2 diabetes mellitus, differed little in 57.5 % of cases from the control group, and only in 42.5 % of the examined individuals its indicators slightly exceeded its norm. Perhaps these data express a weak compensatory increase in the intensity of bone formation against the background of the absence of an active destructive process in periodontal tissues (on average 16.6 ± 0.6 mg/ml and 19.5 ± 0.4 mg/ml; $p < 0.05$) in the named contingent A large spread of individual BGLAP indicators in representatives of the II comparison group, in general, characterizing the processes of osteogenesis as sufficient in the greater half; in others, it is at a significantly lower level.

It was not possible to establish reliable differences in TRACP in patients of the I and II main groups. Naturally, during the study of TRACP, lower concentrations were found in all patients of the I and II comparison groups, the maximum decrease in its concentration was verified only in 50 % of cases, and moderately increased in others (on average 6.52 ± 0.2 Units/l).

When determining the level of tartrate-resistant alkaline phosphatase, it was found that the largest quantitative deviations of its parameters from physiological levels occurred in patients with rapidly progressive generalized periodontitis (main group I), which indicated a pronounced increase in bone resorption in the mentioned faces. At the same time, it is worth noting that the revealed values of TRACP in the analyzed patients were determined depending on the severity of changes in the density of bone tissue.

In the group of patients with rapidly progressive and chronic generalized periodontitis, without accompanying systemic osteoporosis (comparison group I and II), only tendencies towards a certain increase in the content of TRACP in blood serum were determined in 48 % and 40 % of subjects, in others this indicator approached the upper limits of

the norm. while in others it corresponded to the level of healthy people (on average 5.3 ± 0.2 units/l).

Analysis of changes in TRACP in patients of the II comparison group, who suffered from chronic generalized periodontitis, with established non-active osteoporosis in the bone tissue of the periodontium, revealed a naturally lower increase in TRACP than in all subjects. The concentration of this isoenzyme in comparison with the data of the I-II main groups had a significant difference (4.7 ± 0.2 vs. 6.8 ± 0.2 Units/l and 8.7 ± 0.3 Units/l; $p < 0.05$).

It is worth paying attention to the fact that both in all patients of the I group and in the vast majority of the II primary group (92.9 %), the indicators of TRACP, in contrast to the indicators of the I and II comparative and control groups, had the greatest differences, reflecting a high level of intensity bone resorption in periodontal tissues. This point is a confirmation that the studied marker of bone tissue restoration has a high predictive value for detecting not only the intensity of osteogenesis in the bone tissue of the periodontium, but also in the diagnosis of the severity of generalized periodontitis.

Thus, in patients with generalized periodontitis complicated by diabetes and diabetic osteopathy, differences in the direction and intensity of bone remodeling can be clearly observed, which is confirmed by a more significant decrease in formation markers and a simultaneous increase in resorption markers.

Conclusions. The peculiarity of the clinical course of generalized periodontitis in type 2 diabetes mellitus, burdened by diabetic osteoporosis, is caused and manifested by a decrease in the bone structures of the periodontium in the processes of osteosynthesis and an increase in the intensity of bone resorption.

A feature of the manifestation of rapidly progressive and chronic generalized periodontitis in diabetic osteopathy and without systemic pathology is the increase, independent of the clinical picture of the disease, of signs of osteoporosis activation and a decrease in osteosynthesis in the bone structure of the periodontium, which lead to a significant decrease in the density of bone tissue in the alveolar sprouts.

In order to verify the activity of osteosynthesis and bone resorption in periodontal tissues, the following are of predictive value: diagnosis of different directionality and intensity of bone remodeling based on the levels of the quantitative content in the blood serum of the activity markers of the isoenzyme of the bone fraction of alkaline phosphatase (BAP), BGLAP and the concentration of C-terminal telopeptides (β -Cross-Laps), as well as resistant acid phosphatase tartrate (TRACP).

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