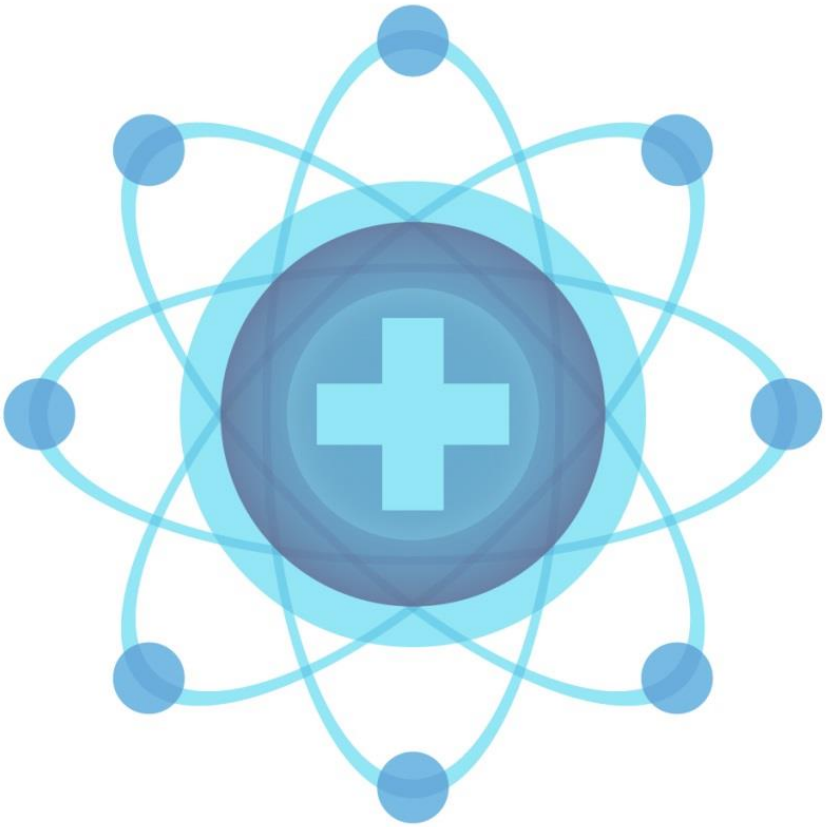

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# Dynamics of markers of bone metabolism in the oral fluid in patients with diseases of the cardiovascular system in preparation for dental implantation

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**Abstract.** The purpose of this study was to study the dynamics of markers of bone metabolism in the oral fluid in patients with diseases of the cardiovascular system in preparation for dental implantation. A total of 74 patients with chronic generalized periodontitis and concomitant diseases of the cardiovascular system and with partial secondary adentia (absence of 1-2 teeth, duration of dentition defect up to 1 year) were examined before dental implantation. oral fluid in patients with chronic periodontal pathology and combined disease of the cardiovascular system during the preparation of dental implantation is statistically significant, indicating the state of the alveolar bone and hard tissues of the teeth on the contact and cervical surfaces.
**Keywords:** alkaline phosphatase, osteocalcin, hydroxyproline, calcium, phosphorus, oral fluid, urine

**Introduction.** As you know, the success of dental implantation is associated primarily with the osseointegration of implants, their survival and long-term functional constancy. Meanwhile, a very important condition for bone restoration and osseointegration of dental implants is the normal functioning of the bone tissue, which is ensured by the balance between the interrelated processes of bone resorption and its formation. The noticeable influence of osteocytes and immune cells has recently been widely discussed as a key regulatory moment in the osseointegration of a dental implant. Changes in homeostasis that occur during the development of inflammatory and destructive processes in the maxillofacial region can affect the biochemical parameters of the oral fluid, which, along with other compounds, contains a system of enzymes that activate various osteogenesis processes. According to the literature, based on the dynamics of the parameters of the oral fluid (OC), one can judge the activity and completeness of the processes of bone tissue regeneration, and the analysis of specific components in the OC reflects the state of the periodontium around the implant, including the development of the inflammatory process in soft tissues. Alkaline and acid phosphatase levels are one of the markers that allow assessing the processes of bone tissue regeneration. Alkaline phosphatase plays a key role in mineralization by breaking down inorganic pyrophosphate and releasing free inorganic phosphate. It is believed that this enzyme can also be used as a biochemical marker to determine the activity of osteoblasts, since it is present on fragments of their plasma membranes. One of the important markers of bone metabolism is osteocalcin, which is a non-covalent calcium-ion binding protein, also known as y-

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carboxyglutamic acid protein, produced by both osteoblasts and odontoblasts. Osteocalcin binds hydroxyapatite and calcium during the mineralization of the organic matrix. It is one of the serological markers in the process of bone formation. Found that osteocalcin plays an important role in the formation and metabolism of bone tissue. It should be noted that in many studies, blood was the material for studying the processes of reparative bone regeneration, and very little information is available on the determination of the above parameters in gastric cancer. To date, there are limited studies examining bone metabolism around dental implants, the consequences and complications of dental implantation, and most of these studies are experimental in nature. Most researchers believe that the use of alkaline phosphatase and osteocalcin as potential indicators of the activity of reparative and destructive inflammatory processes requires more detailed study. Based on the foregoing, the purpose of this study was to study the dynamics of markers of bone metabolism in the oral fluid in patients with diseases of the cardiovascular system in preparation for dental implantation.

## Material and research methods

We examined 109 people aged 40 to 60 years, all patients showed signs of chronic generalized periodontitis (CGP). In accordance with the objectives of the study, 3 groups were formed: Group I - 50 patients (39 men and 11 women) with chronic generalized periodontitis against the background of AH and IHD: exertional angina pectoris II-IV functional class (according to the Canadian classification), aged 43 to 60 years. Group II - 34 patients (22 men and 12 women) with CGP on the background of AH and coronary artery disease combined with adentia who are at the stages of treatment for CVD, Group III - 25 patients (15 men and 10 women) with periodontal pathology (CGP), without diseases of the cardiovascular system (CVS) at the age of 40 to 60 years. It was mandatory for all study participants to read and sign an informed consent approved by the local ethics committee of the Ministry of Health of the Republic of Uzbekistan. It should be noted that all patients included in the groups were examined by a cardiologist. To clarify the diagnosis of coronary artery disease, all patients underwent physical and instrumental examination: ECG at rest in 12 conventional leads, two-dimensional echocardiography, coronary angiography, 24-hour blood pressure monitoring, 24-hour Holter monitoring and laboratory studies. All patients were examined by a dentist. A standard clinical dental examination was carried out: assessment of patient complaints, medical history and life, objective status, assessment of periodontal indices. The level of individual hygiene and the condition of periodontal tissues were assessed in all patients. The hygienic state of the oral cavity was determined by the Green-Vermillion (OHI-S) method (Simplified Oral Hygiene Index). The depth of the periodontal pocket (PC) and the

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loss of the periodontal attachment (PZP) were measured. Gingival bleeding was assessed using H.R. Muhleman. Tooth mobility was determined using the Miller scale (modified by T.J. Fleszar). To identify the developed forms of periodontal pathology, the periodontal index was used (PI, Rüssel, 1956); the degree of gingival recession according to P.D. Miller (1985).

Oral fluid (OR), which was collected on an empty stomach, from 8.00 to 9.30 was used as a biological material. The activity of alkaline phosphatase and the content of osteocalcin in the gastric fluid were measured by ELISA using diagnostic test kits from Hoffmann-LaRoche (Switzerland). To study calcium-phosphorus metabolism, the daily excretion of calcium and phosphorus in the urine was determined. The calcium content was determined in daily urine by the Greenblatt and Hartman method. Determination of inorganic phosphorus in daily urine was carried out according to the method of O.A. Bodansky (1978). The excretion of free hydroxyproline in daily urine was carried out according to the method of Neumann and Logan modified by P.N. Sharaeva (2002).

Statistical processing of the obtained data was carried out using standard software packages Statisticaversion7.0 (USA). Differences in comparison of mean values in paired comparisons were considered significant when _p <0.05.

Research results and their discussion

When analyzing the dental status of patients, more pronounced changes in the periodontal index were found, which indicates inflammatory processes in the periodontium of patients of the first and second observation groups. The average value of the PMA index in the observation group was 63% (in the comparison group - 34%), the periodontal index Russel-PI = 4.9 ± 0.3 (in the comparison group - 1.4 ± 0.1). The PBI bleeding index in the observation group is almost three times higher than in the comparison group (3.1 and 1.1, respectively), although the mean values of the OHI-S hygiene index in patients of the observation group and the comparison group differ insignificantly: 2.5 and 2.3 ...

The main factor affecting the state of the periodontium in patients without concomitant pathology is the hygienic state of the oral cavity. The values of hygiene indices in the observation group were statistically significantly higher than in the comparison group, which indicated a deterioration in the state of oral hygiene. Based on the complaints identified, it should be assumed that the majority of patients with coronary heart disease have bleeding gums; they

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associate this with the intake of antiplatelet agents and anticoagulants, and not with unsatisfactory hygienic care. The analysis of the obtained research results showed that the majority of patients of group I complained of gum bleeding (spontaneous, when eating and brushing teeth) - 57.9%. In group II patients, bleeding of the gums was observed only in 68.7%. Pain sensations when chewing food and brushing teeth were more often observed in patients of group II - 69.4%, in group II - 20%. No less characteristic complaint in generalized periodontitis is the mobility of the teeth, so. Group I patients noted this symptom in 65.1% of cases, versus 72% of Group II patients.

Table 1

Patient complaints

| | Group I patients n = 50 | Group II patients n = 34 | Comparison group n = 25 |
|---|---|---|---|
| Bleeding gums | 31 (61%) | 28 (83%) | 6 ( 25%) |
| Painful sensations (when experiencing food, brushing teeth) | 26 (52%) | 24 (71%) | 4 (17%) |
| Tooth mobility | 27 (54%) | 23 (67%) | 5 (18%) |
| Dry mouth | 31 (62%) | 27 (78%) | 10 (39%) |
| Burning tongue | 15 (29%) | 12 (34%) | 5 (18%) |
| Smell from the mouth | 38 (76%) | 28 (84%) | 11 (42%) |

Thus, all patients of groups I and II presented complaints. associated with periodontal damage. The study of periodontal pockets revealed that in patients of group I, the average value of the pocket depth was 3.7 ± 1.5 mm. in patients of group II - 4.1 ± 0.3. To assess the state of the periodontium, the CPITN index was calculated. These tables show that more severe periodontal damage is observed in the second group than in the first group of patients, this is shown by the high values of the CPITN index. Analysis of the OHI-S hygiene index (G&V) shows that higher values are noted in both the first and second groups. The PI index, which reflects the severity of periodontal lesions, is 3.9 ± 0.5 in the first group, and 4.1 ± 0.3 in the second group. At the same time, the maximum value of the PI index was noted in CGP against the background of coronary artery disease with

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combined adentia. It is 4.1, which corresponds to a moderate-severe degree of chronic generalized periodontitis.

Alkaline phosphatase levels are one of the indicators that allow assessing the processes of bone tissue regeneration. It was found that this enzyme is involved in the regulation of phosphorus-calcium metabolism. Alkaline phosphatase plays a key role in mineralization by breaking down inorganic pyrophosphate and releasing free inorganic phosphate. It is believed that this enzyme can also be used as a biochemical marker to determine the activity of osteoblasts, since it is present on fragments of their plasma membranes. Alkaline phosphatase is directly involved in the implementation of the phagocytic function and its level changes depending on the severity of the inflammatory and necrotic process of the tissue. The data we obtained, presented in table 2, indicate the inhibition of the enzyme activity in the examined persons of groups 1 and 2 relative to the indicators of the comparison group. As you know, one of the important markers of bone metabolism is osteocalcin, which is a non-covalent calcium-ion binding protein produced by both osteoblasts and odontoblasts. Osteocalcin binds hydroxyapatite and calcium during the mineralization of the organic matrix. The analysis of the obtained research results showed that in patients of the 1st group the content of osteocalcin in the oral fluid increased insignificantly, while in the patients of the 2nd group the increase in osteocalcin was significantly higher - on average by 26% relative to the indicators of the comparison group. The increase in the levels of osteocalcin in the oral fluid in the examined persons with concomitant pathology indicated the formation and metabolism of bone bone tissue. A comparative analysis of the study results regarding the excretion of oxyproline in daily urine revealed an increase in this indicator in the main group compared with the comparison group. So the indicators of hydroxyproline in urine in patients of group 1 exceeded the initial level by 14%, while this indicator in patients of group 2 averaged 81.63 ± 5.33 μmol / l, which is 38% higher than the indicators of the comparison group.

Table 2

Indicators of markers of bone metabolism in patients with the disease cardiovascular system in preparation for dental implantation

| Indicators | Group III Comparisons n = 25 | The patients I-groups n = 50 | The patients II-groups n = 34 |
|---|---|---|---|
| Alkaline phosphatase in the oral fluid U / L | 28,98 ± 1,21 | 27,17 ± 1,14 | 25,02 ± 1,03* |

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| | | | |
|---|---|---|---|
| Osteocalcin in the oral fluid U / L | 0,73 ± 0,05 | 0,81 ± 0,07 | 0,92 ± 0,08* |
| Free hydroxyproline in urine, μmol / l | 59,17 ± 4,03 | 67,24 ± 4,89 | 81,63 ± 5,33* |
| Calcium content in urine, μmol / l | 2,28 ± 0,19 | 2,59 ± 0,17 | 3,34 ± 0,21* |
| Phosphorus content in urine, μmol / l | 21,03 ± 1,42 | 23,58 ± 2,07 | 27,12 ± 1,62* |

Note: *- reliability of differences P <0.05 relative to the group comparisons

When analyzing the elemental composition of urine in the examined individuals, it was found that the average indicators of calcium concentration in the urine in patients of group 1 relative to the indicators of the comparison group increased by 14% and amounted to 2.59 ± 0.17 μmol / l versus 2.28 ± 0.19 μmol / l. In the group of patients with concomitant pathology against the background of adentia, the average was 3.34 ± 0.21 μmol / l, which is 46% higher than the initial values.

The average indicator of the level of phosphorus in urine in patients of group 1 increases to 23.58 ± 2.07 μmol / l, which is 12% more than in the comparison group. In patients with chronic periodontal pathology and combined disease of the cardiovascular system against the background of adentia, the studied indicator was 27.12 ± 1.62 μmol / l , which is 29% higher than the initial indicators.

Thus, the results of a comprehensive assessment of the metabolic state of bone tissue in patients with chronic periodontal disease and combined cardiovascular pathology indicate a systemic impairment of the remodeling of the alveolar bone of the jaw, depending on the severity of the underlying and concomitant pathology. The pathological changes are based on increased resorption of bone tissue and suppression of the processes of its formation. At the same time, the biochemical parameters of the oral fluid and urine of the examined patients allow us to assess the intensity of damage to soft tissues, alveolar bone and hard tissues of teeth on the contact and cervical surfaces.

## Conclusions

1. A decrease in alkaline phosphatase activity and an increase in osteocalcin in the oral fluid in patients with chronic periodontal pathology and combined disease of the cardiovascular system during the preparation of dental implantation is statistically significant, indicating the state of the alveolar bone and hard tissues of the teeth on the contact and cervical surfaces.

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2. The content of hydroxyproline, calcium and phosphorus in urine was increased relative to the comparison group. The revealed features of mineral mineral metabolism in patients with combined pathology confirm the possibility of the development of osteopenic syndrome in the examined individuals.

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