Research Article

Pharmacological correction of the activity of bone remodelling markers in the oral fluid of patients with generalised periodontitis depending on blood type

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Abstract

This article presents the data on the effectiveness of the treatment complex we developed on the activity of bone remodelling markers in the oral fluid during the treatment of generalized periodontitis, depending on the blood group. The use of our proposed drugs of general and local action in patients with generalized periodontitis of different blood groups allowed to reduce the average content of TRACP in the oral fluid by 18.25%, while increasing the level of BSALP by 27.64% in comparison with the corresponding data before treatment, p, p_1<0.05, 0.01, which indicates the predominance of bone remodelling processes over osteoresorption processes in patients of the main group. The tactics of treatment of patients with generalized periodontitis of different blood groups, which we propose, is more effective than the conventional therapy and contributes to a faster achievement of remission of generalized periodontitis.

Keywords

Introduction

A special place in the structure of dental morbidity is occupied by the pathology of the periodontal complex, in particular, chronic generalized periodontitis, which, according to the WHO, is the second most common of all dental diseases, second only to caries (Lysokon et al. 2022). Solving the problem of timely diagnosis, prevention and treatment of periodontal pathology is still the most urgent task of modern dentistry (Demkovych et al. 2023). Generalized periodontitis (GP) is not only a focus of chronic infection and a source of sensitization of the body, but also the main cause of tooth loss (especially in older age groups), which leads to serious destructive consequences and disorganization of the dentition (Hasiuk et al. 2017). This fact can seriously affect the quality of human life, making periodontal disease not only a medical problem, but also a social one (Cekici et al. 2014).

PENSOFT.

Markers of bone metabolism have found wide diagnostic applications in dentistry. It is particularly relevant today to improve the efficiency of diagnosis, treatment and prevention of periodontal diseases, namely generalized periodontitis (López-Lacomba 2017). Despite the variety of etiological factors of generalized periodontitis that have been established to date, bone metabolism disorders should be recognized as one of the central mechanisms of the pathogenesis of generalized periodontitis, because osteoporotic changes in the alveolar bone, resorption of its cortical layer and atrophy of the interdental septa are considered pathognomonic signs of the disease (Avdeev et al. 2022).

Today, noninvasive diagnostic methods occupy a modest place, but the importance of such methods and biological objects obtained noninvasively in the clinic in the medicine of the future can hardly be overestimated (Bandrivskaia et al. 2014). Interest in the study of the composition and functions of oral fluid has recently led to the accumulation of new factors that reveal the high regulatory and trophic potential of this biological environment and the versatility of its protective mechanisms (Zabolotny et al. 2016).

At present, there is practically no real database for individualizing the molecular basis of metabolism by some parameters, one of which is genetically determined by blood type.

Given that our previous studies have identified the peculiarities of the course of generalized periodontitis depending on blood type, namely a correlation between markers of bone remodelling in blood and oral fluid, which in turn allowed the use of oral fluid as an alternative to blood in laboratory tests during the diagnosis and evaluation of the effectiveness of treatment of generalized periodontitis (Bandrivsky et al. 2023). This article presents the data on the effectiveness of the therapeutic complex developed by us on the activity of bone remodelling markers in oral fluid during the treatment of generalized periodontitis depending on blood type.

Objective. To evaluate the effectiveness of our proposed treatment complex based on the dynamics of bone remodelling markers in the oral fluid of patients with generalized periodontitis of different blood groups.

Materials and methods

In our study, 106 patients with generalized periodontitis were examined and treated. The patients of the study groups were divided into two groups – the main group and the control group, and within each group the patients were divided into subgroups according to blood group and severity of generalized periodontitis. Thus, the main group included 56 patients with generalized periodontitis divided into 4 subgroups: 1A – 18 patients with blood group 0 (I) (32.14%); 2A – 16 patients with blood group A (II) (28.57%); 3A – 12 patients with blood group B (III) (21.43%) and 4A – 10 patients with blood group AB (IV)

(17.86%). The control group consisted of 50 patients, also divided into 4 subgroups: 1B – 16 patients with blood group 0 (I) (32.0%); 2B – 14 patients with blood group A (II) (28.0%); 3B – 10 patients with blood group B (III) (20.0%) and 4B – 10 patients with blood group AB (IV) (20.0%).

The appointment of drugs was carried out depending on the blood type of patients and the degree of generalized periodontitis. Considering the data obtained in our previous studies (Bandrivsky et al. 2022), namely changes in metabolic parameters of oral fluid and structural and functional composition of blood cells were of the same type for representatives of blood groups 0 (I) and A (II) and B (III) and AB (IV) with varying severity of generalized periodontitis. Therefore, the treatment was the same, but differed in the dose and frequency of preparations for representatives of blood types 0 (I) and A (II) and B (III) and AB (IV). After completion of treatment, all patients were recommended to undergo maintenance therapy twice a year, which included the use of topical and general medications.

Patients with blood group 0 (I) and A (II) and generalized periodontitis of the first degree were prescribed hydrogel "Gengigel" (RicerFarma, Italy) oral baths (10 ml undiluted) for 7 days; gel "Gengigel" (RicerFarma, Italy) – gingival applications for 7 days; "Imunal" (Lec, Slovenia) – 1 tablet 3 times a day for 14 days. In patients with blood groups B (III) and AB (IV) and generalized periodontitis of grade I, the following treatment was prescribed: hydrogel "Gengigel" (RicerFarma, Italy) oral baths (10 ml undiluted) – for 5 days; gel "Gengigel" (RicerFarma, Italy) – gingival applications for 5 days; "Imunal" (Lec, Slovenia) – 1 tablet 3 times a day for 10 days.

Patients with II degree generalized periodontitis with blood group 0 (I) and A (II) were prescribed "Lactoferrin Defense" rinse (SesDerma, Spain) – instillation in periodontal pockets for 10 days; gel "NBF Gingival Gel" (Nano Cure Tech, South Korea) – gingival applications for 10 days; "Nucleinate" (Kyivmedpreparat, Ukraine) – 1 capsule twice a day with meals for 14 days. Patients with blood group B (III) and AB (IV) and generalized periodontitis of II degree were prescribed "Lactoferrin Defense" rinse (SesDerma, Spain) - instillation in periodontal pockets for 7 days; gel "NBF Gingival Gel" (Nano Cure Tech, South Korea) – gingival applications for 7 days; "Nucleinate" (Kyivmedpreparat, Ukraine) - 1 capsule 2 times a day with meals for 10 days.

Patients with blood groups 0 (I) and A (II) with generalized periodontitis grade III were prescribed "Biorepair Mouthwash Gum Protection" (Biorepair, Italy) – mouth rinses, instillation in periodontal pockets for 10 days; Gel "Perio – AID Protect" (Dentaid, Spain) – gingival applications for 10 days; "Nucleinate" (Kyivmedpreparat, Ukraine) – 1 capsule 2 times per day with meals for 14 days; "Glutamic acid" (JSC "Kyiv Vitamin Plant", Ukraine) – 2 tablets 2 times per day with meals for 14 days. Patients with blood types B (III) and AB (IV) and generalized periodontitis III degree were prescribed "Biorepair

Mouthwash Gum Protection" rinse (Biorepair, Italy) – mouthwashes, instillation in periodontal pockets for 10 days; Gel "Perio – AID Protect" (Dentaid, Spain) – gingival applications for 10 days; "Nucleinate" (Kyivmedpreparat, Ukraine) – 1 capsule 2 times a day with meals for 10 days; "Glutamic acid" (JSC "Kyiv Vitamin Plant", Ukraine) – 1 tablet 2 times a day with meals – for 10 days.

Patients in the control group were treated for generalized periodontitis according to generally accepted methods (Chen 2017).

Tartrate-resistant acid phosphatase (TRACP) activity was determined in oral fluid by enzyme-linked immunosorbent assay using the "Bone TRAP Assay" kit; bone alkaline phosphatase (BSALP) activity was determined by enzyme-linked immunosorbent assay (Bandrivsky et al. 2019) using standard kits from Phyllisit-Diagnostics, Ukraine. The statistical calculation of the results was performed using the application software "Statistica 8.0" (StatSoft, USA) and the package of statistical functions of the program "Microsoft Excel 2010".

Results

As a result of application of pharmacotherapy in patients with GP with blood group 0 (I) of the main group 30 days after treatment (Table 1), there was a significant decrease in the activity of TRACP in oral fluid – by 4.67%, $p<0.05$, $p_1<0.05$, in comparison with the data before treatment. In the control group of patients with generalized periodontitis of the same blood group, in which the disease was treated with traditional therapeutic measures, the values of the analysed parameters in the oral fluid did not differ statistically from the data before the treatment, $p>0.05$.

Table 1. Dynamics of bone tissue remodelling markers in oral fluid of generalized periodontitis patients with blood group 0 (I) in different treatment periods.

Indicators	Before treatment	Terms of treatment		
		1 month after treatment	6 months after treatment	1 year after treatment
TRACP, ng/ml	3.44±0.05	3.30±0.04°°**	3.06±0.03°*	2.82±0.03°*
	3.45±0.05	3.45±0.05	3.54±0.05	3.60±0.06°°
BSALP, ng/ml	2.31±0.06	2.42±0.06	2.94±0.06°*	3.08±0.07°*
	2.31±0.06	2.39±0.06	2.10±0.05	2.00±0.04

Notes:

$$\frac{a}{b} = \frac{\text{values of indicators in patients of the main group}}{\text{values of indicators in patients of the control group}};$$

°$p<0.01$, °°$p<0.05$ – a significant difference in the values of the parameters in the patients of the main group compared to the data before treatment; *$p_1<0.01$, **$p_1<0.05$ – a significant difference in the values of the parameters in relation to the data of patients in the control group.

In 6 months after treatment, patients with GP of the main group with blood group 0 (I) showed a significant improvement in all analysed parameters in oral fluid. We found a decrease in the concentrations of TRACP activity – by 11.05%, $p<0.01$, $p_1<0.01$ against the background of an

increase in the content of BSALP activity in the oral fluid – by 27.27%, $p<0.01$, $p_1<0.01$.

In the patients of the control group, the values of the analysed indicators in the oral fluid 6 months after the observations were not statistically different from the data before the treatment, $p>0.05$.

Twelve months after the treatment, in patients with GP with blood group 0 (I) (main group), the positive dynamics of the values of the analysed markers of bone remodelling in oral fluid was maintained, which was characterized by a significant decrease in the levels of TRACP activity – by 18.02%, $p<0.01$, with an increase in the levels of BSALP activity – by 33.33%, $p<0.01$, $p_1<0.01$ compared to pre-treatment data. At the same time, the values of analysed parameters in patients with GP, where traditional therapeutic measures were used for the treatment of the disease (control group), were equal to the data before treatment, $p>0.05$.

The dynamics of the values of markers of bone tissue remodelling in patients with blood group A (II) after treatment of generalized periodontitis in different treatment periods is shown in Table 2.

Table 2. Dynamics of values of markers of bone tissue remodelling in oral fluid of patients with generalized periodontitis with blood group A (II) during different treatment periods.

Indicators	Before treatment	Terms of treatment		
		1 month after treatment	6 months after treatment	1 year after treatment
TRACP, ng/ml	3.37±0.07	3.17±0.07°°	2.93±0.06°*	2.88±0.05°*
	3.38±0.07	3.31±0.07	3.24±0.07	3.40±0.08
BSALP, ng/ml	2.40±0.05	2.68±0.06**°	2.89±0.07°*	3.09±0.08°*
	2.40±0.05	2.57±0.05	2.40±0.05	2.25±0.04

Notes:

$$\frac{a}{b} = \frac{\text{values of indicators in patients of the main group}}{\text{values of indicators in patients of the control group}};$$

°$p<0.01$, °°$p<0.05$ – a significant difference in the values of the parameters in the patients of the main group compared to the data before treatment; *$p_1<0.01$, **$p_1<0.05$ – a significant difference in the values of the parameters in relation to the data of patients in the control group.

Thus, 1 month after treatment in patients of the main study group, the values of markers of bone remodelling in oral fluid significantly improved, characterized by a decrease in the level of TRACP activity by 5.94%, $p<0.05$, $p_1<0.05$, with an increase in BSALP activity – by 11.67%, $p<0.01$, $p_1<0.05$ compared with the data before treatment.

In the control group, 30 days after treatment, the values of bone remodelling parameters in oral fluid in patients with GP did not change and were equal to those before treatment, $p>0.05$.

Six months after the treatment, the values of markers of bone remodelling in the oral fluid of patients with GP of the main group with blood group A (II) continued to improve, which was due to a decrease in TRACP activity by 13.06%, with an increase in BSALP activity by 20.42%, $p<0.01$, $p_1<0.05$ in comparison with the initial data. In the control group, 6 months after the treatment, the values of

the analysed parameters in the oral fluid of the patients with GP were equal to the data before the treatment, p>0.05.

During 12 months after the treatment in patients with blood group A (II) (main group) the positive dynamics of the values of all analysed parameters in the oral fluid was observed. At the same time, in the oral fluid of patients of the main group, a decrease in the level of TRACP activity – by 14.55% against the background of an increase in BSALP activity – by 28.75% in comparison with the initial data, p<0.01, p_1<0.01, was observed. In the control group, 12 months after the treatment, the values of the analysed parameters in the oral fluid were equal to the values before the treatment, p>0.05.

The study of the activity of bone remodelling markers in the oral fluid of patients with generalized periodontitis with blood group B (III) showed (Table 3) that with the use of the treatment regimen developed by us, which included drugs of general and local action, 30 days after the treatment in the oral fluid of patients in the main group we observed an improvement in the values of markers of bone tissue remodelling, which was characterized by a decrease in TRACP activity by 9.10%, p<0.01, p_1<0.05. In the patients of the control group, in which traditional therapeutic measures were used for the treatment of GP, the values of the studied parameters 1 month after the treatment were equal to those before the treatment, p>0.05.

Table 3. Dynamics of values of markers of bone tissue remodelling in oral fluid of patients with generalized periodontitis with blood group B (III) at different periods of treatment.

Indicators	Before treatment	Terms of treatment		
		1 month after treatment	6 months after treatment	1 year after treatment
TRACP, ng/ml	3.41±0.06	3.10±0.05°**	2.96±0.04°*	2.78±0.03°*
	3.40±0.06	3.27±0.06	3.63±0.05°°	3.74±0.06°
BSALP, ng/ml	2.24±0.07	2.36±0.07	2.48±0.08°°	2.60±0.09°*
	2.23±0.07	2.30±0.08	2.28±0.07	2.19±0.06

Notes:

$$\frac{a}{b} = \frac{\text{values of indicators in patients of the main group}}{\text{values of indicators in patients of the control group}};$$

°p<0.01, °°p<0.05 – a significant difference in the values of the parameters in the patients of the main group compared to the data before treatment; *p_1<0.01, **p_1<0.05 – a significant difference in the values of the parameters in relation to the data of patients in the control group.

Six months after treatment, in the main group of patients with blood group B (III), a significant improvement in the values of markers of bone remodelling in oral fluid was observed, characterized by a decrease in TRACP activity by 13.20%, p<0.01, p_1<0.01, with an increase in BSALP activity by 10.71%, p<0.05, p_1>0.05, in comparison with the pre-treatment data. In the control group, 6 months after treatment, the values of the studied parameters of oral fluid metabolism were equal to the initial data, p>0.05. It should be noted that in the patients of the control group, the activity of TRACP in the oral fluid increased during the study period, which was 6.76% higher than the reference values, p<0.05.

After twelve months of observation, patients with blood group B (III) (main group) maintained positive dynamics of values of analysed parameters in oral fluid. We found an increase in BSALP levels by 16.07%, with a decrease in TRACP activity by 18.48%, p<0.01, p_1<0.01 in comparison with the data before treatment. In patients of the control group, during this research period, the parameters of bone metabolism deteriorated, which was characterized by an increase in the level of TRACP activity in oral fluid – by 10.0%, p<0.01 compared to the data before treatment. The values of BSALP in oral fluid were equal to the initial data, p>0.05.

The study of markers of bone tissue remodelling in the oral fluid in patients with generalized periodontitis with blood group AB (IV) showed (Table 4) that 1 month after treatment there was a decrease in the concentration of TRACP – by 7.31%, p<0.01, p_1>0.05 and an increase in the level of BSALP activity – by 10.82%, p<0.01, p_1<0.05. At the same time, 1 month after the observations in the patients of the control group, where traditional methods of treatment were used for the management of GP, the values of the studied parameters did not change and were equal to the data before treatment, p>0.05.

Table 4. Dynamics of bone tissue remodelling markers in oral fluid of patients with generalized periodontitis of blood group ab (IV) at different treatment periods.

Indicators	Before treatment	Terms of treatment		
		1 month after treatment	6 months after treatment	1 year after treatment
TRACP, ng/ml	3.42±0.06	3.17±0.05°	2.92±0.04°*	2.67±0.03°*
	3.43±0.06	3.41±0.06	3.52±0.07	3.80±0.08°
BSALP, ng/ml	2.31±0.05	2.56±0.05°**	2.85±0.06°*	3.10±0.07°*
	2.30±0.05	2.39±0.05	2.30±0.05	2.21±0.04

Notes:

$$\frac{a}{b} = \frac{\text{values of indicators in patients of the main group}}{\text{values of indicators in patients of the control group}};$$

°p<0.01, °°p<0.05 – a significant difference in the values of the parameters in the patients of the main group compared to the data before treatment; *p_1<0.01, **p_1<0.05 – a significant difference in the values of the parameters in relation to the data of patients in the control group.

In 6 months after the treatment in the main group with blood group AB (IV) a significant improvement of a number of parameters in the oral fluid was found. Thus, we found a decrease in the content of TRACP – by 14.52%, p<0.01, p_1<0.01 and an increase in the level of BSALP activity in the oral fluid – by 23.38%, p<0.01, p_1<0.01. At the same time, in the patients of the control group, the values of the parameters in the oral fluid during this period of research were equal to the initial data, p>0.05.

Twelve months after the study, the patients of the main group, treated with the therapy proposed by us for the treatment of generalized periodontitis, maintained a positive dynamic of the values of the studied parameters in the oral fluid. Thus, a decrease in the content of TRACP in the oral fluid was studied – by 21.93%, p<0.01, p_1<0.01 in comparison with the data before treatment. At the same

time, an increase in BSALP activity was observed – by 34.20%, p<0.01, p_1<0.01 compared to the corresponding baseline values. In the control group, 12 months after the treatment, the values of the analysed parameters in the oral fluid were equal to the values before the treatment, p>0.05.

Discussion

Treatment and rehabilitation of patients with dystrophic-inflammatory diseases of periodontal tissues is one of the most difficult problems in modern dentistry, which is reflected in the large number of pharmaceuticals offered to solve this problem, which are not always effective (Demkovych 2019). Currently, dentists have come to the understanding that in the treatment of inflammatory diseases of periodontal tissues, it is necessary to use methods aimed at restoring both local tissue homeostasis and the entire pathogenetic mechanism of this pathology (Al-Askar et al. 2021). In this regard, periodontists use both local and general therapeutic approaches.

Numerous evidences of the connection between inflammatory lesions of periodontal tissues and the general condition of the body require that the treatment tactics of such patients should be directed not only to elimination of the inflammatory process in the periodontium, but also to correction of the general condition of the body (Hasiuk et al. 2021). Along with the application of modern methods of therapeutic treatment of the affected systems, it is necessary to apply methods of integral multisystem correction at the cellular and molecular level. This is due to the fact that any chronic disease is a defining stage of a long-term pathophysiological process in the body, when the mechanisms of cellular alteration are initiated and mediated by redox reactions, impaired transport and trophic functions, and cytokine regulation with the development of immunopathological processes (Kalashnikov et al. 2020). Understanding the universal pathogenetic role of the above factors motivates their selection as targets for targeted therapeutic interventions in dystrophic-inflammatory lesions of periodontal tissues.

The search for alternative methods to treat inflammatory periodontal disease has led dentists to use antioxidants in periodontics (De Lima et al. 2016). However, in most cases, the tactic of prescribing antioxidants is empirical rather than scientifically based.

The immune system is one of the most sensitive to pathogenic factors (Demkovych et al. 2021). Various disorders of its normal functioning accompany a wide range of internal and dental pathologies. Not only the development, but also the course and consequences of diseases depend on the state of the body's immune reactivity. According to many clinical immunologists (Cekici et al. 2014), in modern medicine, there are obvious prerequisites for revising tactical treatment regimens for pathologies with impaired immune system function. It is necessary to correct and prevent immunological imbalances, which can be manifested by a deficiency of certain parts of the immune system, as well as hyperergic reactions to foreign agents and autoimmune processes. According to (Chen 2017), the basis for prescribing immunomodulators in the presence of an infectious and inflammatory process in a patient should be primarily clinical data, even in the absence of significant abnormalities in laboratory and immunological studies.

Regulation of the secretory function of mononuclear phagocytes with the predominant use of drugs with concomitant detoxifying and antioxidant effects is proposed as a rational tactic in acute inflammatory processes accompanied by excessive release of proinflammatory mediators (Lahdentausta et al. 2018). Antioxidant vitamins, sulphur preparations (sodium thiosulfate) and reamberine are indispensable in this case.

In clinical practice, attempts are made to eliminate the function of proinflammatory cytokines: interleukins-1, -6; tumour necrosis factor, the activity of which increases in acute inflammation (Demkovych et al. 2023). In chronic inflammation it is advisable to use interleukin-2, which is the main factor in the proliferation and differentiation of T lymphocytes, and under certain conditions activates B lymphocytes, as well as cells of the mononuclear phagocytic system. In addition, it reduces the processes of catabolism that occur during inflammatory and destructive processes in tissues (Kostyrenko et al. 2021).

The use of our proposed drugs of general and local action in patients with generalised periodontitis of different blood groups allowed to reduce the average content of TRACP in the oral fluid by 18.25%, while increasing the level of BSALP by 27.64%, compared to the corresponding data before treatment, p, p_1<0.05, 0.01, which indicates the predominance of bone remodelling processes over osteoresorption processes and, in turn, convincingly proves the effectiveness of their use in this contingent of patients. The normalization of the values of bone metabolism in the oral fluid in patients with generalized periodontitis after the application of the proposed therapy (depending on the blood type) was accompanied by the improvement of the clinical condition of the periodontal tissues and is probably one of the main factors directly contributing to this process.

Conclusion

Thus, our proposed tactic of treatment of patients with generalized periodontitis of different blood types is pathogenetically sound and more effective than conventional therapy and contributes to faster achievement of remission of generalized periodontitis.

Acknowledgments

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