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BIOCHEMICAL PARAMETERS OF THE EFFICIENCY OF AUTOPLASMA AND HYALURONIC ACID IN THE COMPLEX TREATMENT OF GENERALIZED PARODONTITIS

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In this study, the dynamics of biomarkers of inflammation and the antioxidant system was assessed. The study involved 57 patients aged 36 to 55 years with a diagnosis of generalized parodontitis. In addition to basic therapy, the complex treatment of patients included regenerative techniques: injection of i-PRF, injection of plasmogel from platelet autoplasma and administration of hyaluronic acid. After the treatment, the most pronounced result of a decrease in the content of malondialdehyde was obtained in the group with a combination of plasmogel, hyaluronic acid and injectable platelet rich fibrin, after 1 year – 0.18±0.01 mmol/L, after 2 years – 0.21±02 mmol/l. In all groups, where the treatment with regenerative drugs was carried out, the activity of the catalase enzyme significantly increased in comparison with the comparison group, $p_2 < 0.001$. The data obtained indicate that the applied regenerative techniques are able to actively affect the antioxidant system and reduce the processes of lipid peroxidation, which are one of the trigger mechanisms for the development and maintenance of inflammation in the parodontal tissues.

Key words: malondialdehyde, catalase, plasmogel, lipid peroxidation, antioxidant system.

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БІОХІМІЧНІ ПАРАМЕТРИ ЕФЕКТИВНОСТІ АУТОПЛАЗМИ І ГІАЛУРОНОВОЇ КИСЛОТИ У КОМПЛЕКСНОМУ ЛІКУВАННІ ГЕНЕРАЛІЗОВАНОГО ПАРОДОНТИТУ

В даному дослідженні проводилася оцінка динаміки біомаркерів запалення і антиоксидантної системи. Обстежено було 57 хворих у віці від 36 до 55-ти років з діагнозом генералізований пародонтит. В комплексне лікування хворих крім базисної терапії були включені регенеративні методики: ін'єкційне введення і-PRF, введення плазмогеля з тромбоцитарної аутоплазми і введення препарату гіалуронової кислоти. Після проведеного лікування найбільш виражений результат зниження вмісту малонового діальдегіду був отриманий в групі з комбінацією плазмогеля, гіалуронової кислоти і збагаченого тромбоцитами фібрину, через 1 рік – 0,18±0,01 ммоль/л, через 2 роки – 0,21±0, 02 ммоль/л. У всіх групах, де проводилося лікування регенеративними препаратами, активність ферменту каталази достовірно збільшилася у відношенні з групою порівняння, p2<0,001. Отримані дані говорять про те, що застосовані регенеративні методики здатні активно впливати на антиоксидантну систему і зменшувати процеси перекисного окислення ліпідів, які є одним з пускових механізмів розвитку і підтримки запалення в тканинах пародонта.

Ключові слова: малоновий діальдегід, каталаза, плазмогель, перекисне окислення ліпідів, антиоксидантна система.

The work is a fragment of the research project: "Correction of metabolic disorders pathogenetic mechanisms in the oral cavity tissues of patients depending on environmental and alimentary factors affecting carbohydrate and lipid metabolism", state registration No. 0118U006966.

Among all inflammatory parodontal diseases, a special place is given to generalized parodontitis, which is a serious medical, social and economic problem. The prevalence of this pathology among adults remains at a high level and does not tend to decrease. [3]. The clinical picture of chronic generalized periodontitis is characterized by weak manifestations and latent course, which complicates timely diagnosis and the beginning of treatment and measures [1].

According to modern concepts, bacterial aggression is one of the factors that initiates the onset of parodontal diseases, determines the development of various forms of inflammation of the parodontal complex, depending on the nature and intensity of the body's response [7]. One common pattern in all types of inflammation is, as a rule, an increase in lipid peroxidation (LPO), which occurs on the background of a decrease in the activity of the physiological antioxidant system (AOS) of the body [6]. One of the main reasons for LPO activation in case of various pathological processes is tissue hypoxia, which occurs as a result of a violation of the ability of tissues to absorb oxygen from the blood or due to a decrease in the efficiency of enzymatic oxidation [9, 11].

In recent studies, the significance of hemoendothelial imbalance of the microvasculature in the pathogenesis of parodontal diseases has been shown. [10].

LPO activation leads to disturbances in tissue respiration in the inner mitochondrial membrane, hydroxylation processes in microsomes, and the release of cytotoxic products from polymorphonuclear leukocytes [8].

A number of studies have established that the parodontium, due to its rich vascularization and innervation, is an object of emotional stress, which activates LPO. This phenomenon is accompanied by the appearance of signs of destruction: vascular dilatation, bone resorption, granulation proliferation. Antioxidant deficiency, excessive accumulation of LPO products leads to a prolonged course of these pathological processes.

Some studies provide evidence that in chronic periodontitis the activity of some types of antioxidant enzymes (catalase, cytochrome oxidase, glutathione peroxidase) decreases in the periodontal tissues, and it was found that the chronic process is usually accompanied by a more pronounced decrease in its activity [12].

Some studies have found a significant increase in the rate of formation of malondialdehyde (MDH) in gum homogenates during inflammation. In patients with parodontitis, the content of MDH in the blood of the vessels of the gums of the oral cavity increases in direct proportion to the severity of the disease. The output background of the disease determines the main risk factors for AOS deficiency, which leads to the development of acute hypoxia of parodontal tissues, activation of lipid peroxidation processes and diffusion of products from soft tissues into bone tissue, induces the destruction of collagen fibers and osteoporosis of the jaw bones.

The high prevalence of periodontal diseases dictates the need to search for optimal treatment methods, taking into account the pathogenetic mechanisms of development, therefore, the search for new means of protecting periodontal tissues from the pathological effects of LPO products is an urgent task.

The purpose of the study was to research the dynamics of biomarkers of inflammation and the antioxidant system in the conservative treatment of generalized parodontitis using autoplasma and hyaluronic acid preparations**.**

Materials and methods. This study is based on the analysis of our own data obtained as a result of examining 57 patients aged 36 to 55 years with a diagnosis of generalized parodontitis of II – III degrees of severity, chronic course. To assess the effectiveness of the proposed treatment regimens, the patients were divided into 4 groups, one comparison group and 3 main. The basic therapy was the same for all groups: smoothing of the root surface with antiseptic treatment of the oral cavity with 0.12% chlorhexidine digluconate solution. Dental plaque was removed with a "Sonyflex" sonic instrument, a "Prophiflex" (KaVo, Germany) hendiblaster, using a glycine-based powder – Perio (KaVo). Smoothing of the root surface was performed using Gracie zone-specific curettes (Hu-Friedy) [2].

All groups of patients received basic therapy, and each group also received different combinations of autoplasma and hyaluronic acid preparations. 2nd group received 5 procedures of injection of fibrin (i-PRF), with an interval of every 7 days, and instillation of hyaluronic acid into the periodontal pocket 0.2 g once. 3rd group received plasmogel 3 procedures with an interval of 7 days and once instillation of hyaluronic acid. 4th group received plasmogel 3 procedures with an interval of 7 days, instillation of hyaluronic acid and every 6 months in the form of maintenance therapy with i-PRF injections, 5 procedures every 7 days.

Sterile vacuum tubes (*MM Medic*, Ukraine) and a centrifuge ("ELMI", Latvia) were used to obtain preparations from autoplasma.

Platelet autoplasma i-PRF was obtained by taking blood from a patient's vein with a sterile intravenous catheter into a sterile, free of any impurities tube, which was placed in a centrifuge. Centrifugation protocol at temperature T=+22±2° C, 1000 G, time 5 min.

To obtain a plasmogel from platelet autoplasma, the patient's blood was also collected in a sterile vacuum tube that contained sodium heparin and a separating gel. Centrifugation protocol at temperature T=22±2°C, 3000 revolutions, time 5 minutes. The plasma fraction after centrifugation was taken with a syringe, which was placed in a TDB-120 thermostat, at a temperature of + 80° C, exposure for 7 minutes,

the resulting plasmogel was cooled at room temperature for 10 minutes and inserted into the parodontal pocket using a blunt needle, after which the parodontal dressing Reso-Pac was applied.

HyaDENT BG hyaluronic acid preparation, which contains: hyaluronic acid -- 2 mg, cross-linked hyaluronic acid -- 16 mg, sodium chloride -- 6.9 mg, water for injection up to 1.0 mg. Manufacturer: BioScience GmbH, Germany. Certificate of Conformity No. UA.TR.039.343, date of issue - 18.04.201

Before starting treatment, all patients were trained in hygienic oral care, which included daily 2-fold brushing of teeth using: GUM "ActiVital" toothpaste and rinse aid (SUNSTAR, Japan), "Supreme" toothbrush (TePe, Sweden) and interdental brushes, matched to size. The dynamics of treatment results was assessed: before treatment, after 1 and 6 months, and long-term results after one and two years after the course. Every 6 months, patients of all groups underwent professional hygiene. All patients gave written consent to conduct treatment according to the indicated schemes, in accordance with the requirements of the Commission on Bioethics SE "ISMFS NAMS".

For biochemical studies, the oral fluid of patients was taken [5].

The presence of inflammation in the tissues was assessed by LPO, which was assessed by the MDH content using the reaction with thiabarbituric acid by the method of Stalnaya, Garishvili (1977).

The state of AOS was accessed by the activity of catalase, which was determined by the method of Korolyuk, Ivanova [4].

The results were processed by variational statistical methods of analysis on an IBM PC in SPSS SigmaStat 3.0 and StatSoft Statistica 6.0.

Results of the study and their discussion. The results of biochemical studies of the oral fluid of patients with generalized parodontitis are presented in tables 1-2.

Table 1 shows the dynamics of the MDH content index for all observation periods. From the data obtained as a result of the study, it is possible to estimate the level of the inflammation marker MDH, which reflects the intensity of LPO. The intensity of lipid peroxidation as an indicator of the severity of inflammation before treatment was significantly higher (0.76±0.05 mmol/l) relative to the norm (0.20±0.02 mmol/l).

Table 1

Dynamics of the MDH indicator in the oral fluid (norm 0.20 ± 0.02 mmol/l)

Groups / Terms	Comparison group n=15	Group I Main i-PRF (5 procedures) + 1 HA instillation n=15	Group II Main Plasmogel (3 procedures) + HA n=13	Group III Main Plasmogel + HA 1 instillation + i-PRF (5 procedures) every 6 months n=14
Before treatment n=57	0.76±0.05 p<0.001			
1 month after treatment	0.43±0.03 p<0.001 p_1<0.001	0.22±0.02 p>0.5 p_1<0.001 p_2<0.001	0.48±0.03 p<0.001 p_1<0.001 p_2>0.9	0.46±0.03 p<0.001 p_1<0.001 p_2>0.8
6 months after treatment	0.39±0.02 p<0.001 p_1<0.001	0.23±0.03 p>0.5 p_1<0.001 p_2<0.001	0.36±0.03 p<0.001 p_1<0.001 p_2>0.5	0.34±0.02 p<0.001 p_1<0.001 p_2>0.7
1 year after treatment	0.35±0.02 p<0.001 p_1<0.001	0.25±0.02 p>0.1 p_1<0.001 p_2<0.01	0.36±0.03 p<0.001 p_1<0.001 p_2>0.8	0.18±0.01 p>0.7 p_1<0.001 p_2<0.001
2 years after treatment	0.40±0.03 p<0.001 p_1<0.001	0.24±0.02 p>0.2 p_1<0.001 p_2<0.001	0.31±0.03 p<0.01 p_1<0.001 p_2<0.05	0.21±0.02 p>0.8 p_1<0.001 p_2<0.001

Note: p – index of the reliability of differences from the norm; p_1 – index of the reliability of differences from "before treatment" values; p_2 – index of the reliability of differences from comparison group.

From the presented data, it can be seen that a decrease in the indicator after the treatment took place in all groups (p_1<0.001).

Parodontitis is characterized by an increase in free radical processes. Free radical attack on biological membranes, including mitochondria, causes their damage and disruption of bioenergetic function, increases energy deficit. With parodontitis, not only collagen fibers are destroyed, but also thin fibrils. That is why they become available to the action of proteases that cause their degradation.

The minimum MDH content in the early stages after the treatment was noted in the group of patients who received 5 i-PRF procedures along the transitional fold in the area of projection of the roots of the teeth and 1 injection of hyaluronic acid into the parodontal pocket: after 1 month -- 0.22±0.02 mmol/l, after 6 months -- 0.23±0.02 mmol/l and in the long-term results of treatment, the indicator remained quite stable after 1 year -- 0.25±0.02 mmol/l and after 2 years -- 0.24±0.02 mmol/l. Which makes it possible to assume the effectiveness of the impact of the injection form on the microvasculature of parodontal tissues,

which contributed to the improvement of trophism, and hyaluronic acid serves as matrix of amorphous substances for the formation of collagen fibers.

In group II, after the treatment, the indicator decreased, but at the same time, the reliability of differences with the comparison group was noted only in the long term (after 2 years, $p_2 < 0.05$). Which makes it possible to assume that with the combination of only a plasma gel from platelet autoplasma and a preparation of hyaluronic acid, since both drugs are more likely to restore the lost elements of the ligamentous apparatus, but at the same time do not contribute to neoangeogenesis, a longer treatment and maintenance therapy time is required to restore the microvasculature and trophism.

The most pronounced result of a decrease in the MDH content in the long-term follow-up was obtained in group III, after 1 year -- 0.18±0.01 mmol/l, after 2 years -- 0.21±0.02 mmol/l. But at the same time, in the same group at the early stages of observation, the indicator remained practically the same as in the comparison group, after 1 month -- 0.46±0.03 mmol/l, after 6 months -- 0.34±0.02 mmol/l. This makes it possible to assume that at the initial observation period in the groups where the plasmogel preparation was used, there was a cellular response to the introduction of autologous material, which the cells used as a biodegradable matrix for the formation of new collagen fibers, after which the inflammatory reaction in the parodontal tissues decreased. The use of i-PRF at the stage of maintenance therapy in this group made it possible to restore microcirculation in parodontal tissues.

Catalase is an enzyme that is involved in the body's metabolism and breakdown of hydrogen peroxide and has powerful antioxidant properties.

Table 2 shows the results of the study of catalase activity at different periods of observation. The activity of catalase in the oral fluid of patients is normally 0.30±0.02 μat/l. In case of generalized parodontitis before the start of treatment, this indicator was 0.06±0.001 μat/l, which indicates a sharp decrease in antioxidant activity in patients with generalized parodontitis. After the complex treatment, the indicator increased in all studied groups $p_1 < 0.001$.

In all main groups, where treatment with regenerative drugs was carried out, the activity of the enzyme catalase significantly increased compared with the comparison group after treatment at all periods of observation, $p_2 < 0.001$. The obtained data indicate that the applied regenerative techniques are able to actively influence the antioxidant system and help to reduce the processes of lipid peroxidation, which are one of the trigger mechanisms for the development and maintenance of inflammation in the parodontal tissues.

Table 2

Dynamics of the index of catalase in the oral fluid (norm 0.30 ± 0.02 μat/l)

Groups / Terms	Comparison group n=15	Group I Main i-PRF (5 procedures) + 1 HA instillation n=15	Group II Main Plasmogel (3 procedures) + HA n=13	Group III Main Plasmogel + HA 1 instillation + i-PRF (5 procedures) every 6 months n=14
Before treatment n=57	0.06±0.001 p<0.001			
1 month after treatment	0.09±0.01 p<0.001 p_1<0.01	0.25±0.01 p<0.05 p_1<0.001 p_2<0.001	0.27±0.01 p>0.2 p_1<0.001 p_2<0.001	0.28±0.01 p>0.4 p_1<0.001 p_2<0.001
6 months after treatment	0.12±0.01 p<0.001 p_1<0.001	0.26±0.01 p>0.1 p_1<0.001 p_2<0.001	0.26±0.02 p>0.2 p_1<0.001 p_2<0.001	0.29±0.02 p>0.6 p_1<0.001 p_2<0.001
1 year after treatment	0.16±0.01 p<0.001 p_1<0.001	0.28±0.01 p>0.4 p_1<0.001 p_2<0.001	0.29±0.02 p>0.8 p_1<0.001 p_2<0.001	0.32±0.02 p>0.6 p_1<0.001 p_2<0.001
2 years after treatment	0.18±0.01 p<0.001 p_1<0.001	0.32±0.01 p>0.4 p_1<0.001 p_2<0.001	0.28±0.02 p>0.5 p_1<0.001 p_2<0.001	0.29±0.01 p>0.8 p_1<0.001 p_2<0.001

Note: p – index of the reliability of differences from the norm; p_1 – index of the reliability of differences from "before treatment" values; p_2 – index of the reliability of differences from comparison group.

In physiological processes, hyaluronic acid is formed on the cell membrane and transferred directly to the extracellular space (matrix). In almost all types of tissues, hyaluronic acid is an essential component of the extracellular matrix [7]. With pathological processes in the parodontal tissues, a large number of fibroblasts are destroyed, and, accordingly, a decrease in the production of its own hyaluronic acid. To restore the extracellular matrix, a hyaluronic acid preparation is used, and when combined with plasma preparations, potentiation of anti-inflammatory and regenerative effects is obtained. Conditions are created for the regeneration of parodontal tissues by reducing the inflammatory process and restoring homeostasis.

The function of fibroblasts in parodontitis can be impaired, as a result of which the process of collagen formation, its properties and structure changes.

There is a change in the function of mast cells of the connective tissue: it will increases the penetration of amorphous substances into the connective tissue.

Traditional treatments of generalized parodontitis mainly include maintaining good oral hygiene and performing professional non-surgical and surgical approaches to address etiological factors. Antibiotics and anti-inflammatory drugs can also be used to eliminate microbial infection and pathological inflammatory process [2, 6].

Oxidative stress in the pathogenesis of parodontitis is the result of a violation of the redox balance of cells and tissues. The ratio of MDH and catalase, which most clearly demonstrate the redox potential, which controls the development of the inflammatory process.

The effects of microcirculation restoration play a significant role in the action of the drugs proposed for use, providing an equilibrium advantage of antioxidant mechanisms, stabilization of cell membranes, and, as a consequence, an increase in tissue resistance to the action of etiopathogenetic factors [3].

New and future approaches will rely more on altering the inflammatory response itself, limiting the activity of pro-inflammatory cells, and enhancing pathways that stop the inflammatory process [9, 11]. The use of autoplasma preparations is spreading in many areas due to its role in healing and as a natural alternative to surgery. The principle of the method lies in the introduction of preparations of platelet autoplasma into the tissue and obtaining the effect of stimulating the natural mechanisms of regeneration, due to the growth factors contained in platelets, which contribute to the regeneration of damaged tissues. The viscous form of i-PRF plasma is used when a local effect is needed and it is necessary to create a depot of active components and ensure their maximum long-term stay in the damaged area. Fibrin is a plasma protein, the spiral structure of the molecule of which is able to unfold and form a fibrin network, which provides skeleton and allows the active components of platelet autoplasma to be retained in the required zone, preventing them from diffusing beyond the injection site. This property of the injection use of i-PRF allows regenerative substances and growth factors to remain as long as possible directly at the point of injection of platelet autoplasma and at the same time stimulate anti-inflammatory and regenerative processes directly in the area of injection. When autoplasma is heated to a specified temperature, protein fractions undergo denaturation, but when plasmogel is introduced into the parodontal pocket, it serves as a kind of building material, since it starts the process of tissue remodeling during biodegradation by cellular elements. Plasmogel does not possess the regenerative properties of native autoplasma caused by growth factors, but it can be used in protocols of combined methods to obtain the most long-term therapeutic effect.

Thus, a comparative analysis of the obtained results of the combined technique of using autoplasma and hyaluronic acid preparations showed its effectiveness in the complex treatment of patients with generalized parodontitis. After the carried out studies, it can be assumed that the effect of the combined use of regenerative techniques is associated with the multidirectionality of their action on various structures of the pariodontal complex. However, this hypothesis should be confirmed by further clinical and functional studies.

Conclusion

The obtained results showed that the use of the combined technique of platelet autoplasma preparations and hyaluronic acid preparation led to a decrease in inflammation in all studied groups. The activity of catalase, which possesses powerful antioxidant properties, significantly increased after the complex treatment in the studied treatment groups. Plasmogel from platelet autoplasma is a matrix basis for filling the parodontal pocket, hyaluronic acid has a proper anti-inflammatory effect and acts as an intercellular matrix, and the injection form of platelet autoplasma starts the processes of restoring microcirculation and activating regenerative processes, due to the growth of the presence of platelet factors. The most reliable results in the long-term follow-up were obtained in the first and third groups, which makes it possible to recommend a complex that includes an autoplasma preparation plasmogel, a preparation of hyaluronic acid and an injection preparation of autoplasma i-PRF, which have a pronounced anti-inflammatory and antioxidant effect for use in the complex treatment of generalized parodontitis. These conclusions are based on the results of biochemical studies, but the issues of pathogenetic treatment and regenerative therapy continue to develop and improve in treatment regimens and methods, therefore, they provide potential for further research.

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NON-INFECTIOUS COMPLICATIONS OF TOTAL HIP ARTHROPLASTY THAT ARE NOT ASSOCIATED WITH INSTABILITY OF COMPONENTS

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We analysed outcomes of 369 cases in 364 patients with complications after total hip arthroplasty. In this study we focused on cases with non-infectious complications of total hip arthroplasty that are not associated with instability of components which included prosthetic head dislocations, paraarticular heterotopic ossification, periprosthetic fractures of the femur, pain in replaced joint (not associated with the instability). The effectiveness of surgical elimination of the dislocations was significantly higher compared to the closed reposition. The only efficient method to manage heterotopic ossification was its prompt removal. Open reposition, followed with metal osteosynthesis, was the only effective remedy for 100% of periprosthetic fractures. In case of vertebrogenous pain syndrome, the best results had patients with lesions of posterior column of the lumbar spine.

Keywords: hip joint, complications of arthroplasty, dislocation, heterotopic ossification, periprosthetic fracture, revision prosthetics.

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НЕІНФЕКЦІЙНІ УСКЛАДНЕННЯ ЕНДОПРОТЕЗУВАННЯ КУЛЬШОВОГО СУГЛОБА, ЩО НЕ ПОВ'ЯЗАНІ З НЕСТАБІЛЬНІСТЮ КОМПОНЕНТІВ

Ми проаналізували результати 369 випадків у 364 пацієнтів з ускладненнями після тотального ендопротезування кульшового суглоба. У цьому дослідженні ми зосередили увагу на випадках з неінфекційними ускладненнями тотальної ендопротезування кульшового суглоба, які не пов'язані з нестабільністю компонентів, які включали вивихи голівки ендопротеза, параартикулярну гетеротопічну осифікацію, перепротезні переломи стегнової кістки, біль у оперованому суглобі (не пов'язаний з нестабільністю). Ефективність хірургічного усунення вивихів була значно вищою порівняно із закритою репозицією. Єдиним ефективним методом лікування гетеротопічної осифікації було її швидке видалення. Відкрита репозиція з подальшим остеосинтезом була єдиним ефективним засобом для 100% перипротезних переломів. У разі вертеброгенного больового синдрому найкращі результати мали пацієнти з ураженням заднього стовпа поперекового відділу хребта.

Ключові слова: кульшовий суглоб, ускладнення ендопротезування, вивих, гетеротопічна осифікація, перипротезний перелом, ревізійне ендопротезування.

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Due to the wide implementation of total hip arthroplasty (THA) into clinical practice, the number of associated mistakes and complications is constantly growing. According to different authors, their frequency ranges from 7 % to 30 %. The most commonly encountered are: aseptic instability of components, prosthetic head dislocations, heterotopic ossification, periprosthetic femur fractures, infectious complications [1].