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ПАТОГЕНЕТИЧНЕ ОБҐРУНТУВАННЯ ЗАСТОСУВАННЯ МЕТОДИКИ I-PRF ПРИ ЛІКУВАННІ ГЕНЕРАЛІЗОВАНОГО ПАРОДОНТИТУ ЗА ДАНИМИ ДОСЛІДЖЕННЯ НАУКОВОЇ ЛІТЕРАТУРИ

Мета дослідження. *провести аналіз сучасних літературних даних необхідності та доцільності методики PRF для лікування генералізованого травматичного пародонтиту хронічного перебігу. Вивчення супра (гіпер) контактів та наявність травматичної оклюзії може підтримувати ініціацію хронічного запалення у маргінальному періодонті на фоні порушення бар'єрної функції епітеліального прикріплення та поширеного порушення мікроциркуляції. Місцеве антибактеріальне лікування, проведення професійної гігієни ротової порожнини лише короткочасно знімає симптоми запалення. У зв'язку з цим необхідні дослідження, що визначають можливості аутоімунних компетентних клітин, що мають імунокорелятивні здібності для підтримки місцевого імунного статусу в пародонті. Даний короткий огляд літератури використання імунокомпетентних клітин – тромбоцитів як ключових регуляторів запалення та імунорегулюючих факторів усередині судинного гомеостазу для підтримки місцевого імунного статусу. Дано сучасну патофізіологічну оцінку застосування методик PRF та i-PRF, факторів зростання тромбоцитів для створення колагену I типу, який відіграє провідну роль у репарації. Звертається увага на те що макрофаги в осередках запалення відіграють особливу роль у виробленні факторів росту, таких як тромбоцитарний фактор росту (PDGF), трансформуючий фактор росту ендотелію (TGF), які є також джерелом хемотаксису для стимуляції ангіогенезу. Було визначено, що i-PRF може сприяти функціональній диференціації клітин, подібних до остеобластів, ніж інші клітини крові. Культура i-PRF впливає на здатність первинних остеобластів людини до проліферації, диференціації, мінералізації команд адгезії та міграції. У порівнянні після введення PRF та i-PRF індукується триразове підвищення людських остеобластів та процесів проліферації. Шкідливий вплив на життєздатність клітин, метаболічну активність та міграцію клітин спостерігається, коли концентрація i-PRF перевищувала 60%. Ці дослідження стосуються клінічного значущої теми, пов'язане з лікуванням хронічного пародонтиту і отримана нехірургічними методами регенеративних процесів у пародонтальному комплексі, що має значення для клінічної практики стоматологів.*

Ключові слова: *травматичний пародонтит, тромбоцитарні фактори, PRF, i-PRF, VEGF, місцевий імунітет.*

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PATHOGENETIC SUBSTANTIATION OF THE APPLICATION OF THE I-PRF TECHNIQUE IN THE TREATMENT OF GENERALIZED PERIODONTITIS ACCORDING TO THE RESEARCH DATA OF THE SCIENTIFIC LITERATURE

The purpose of the study*. To conduct an analysis of modern literary data on the necessity and expediency of the PRF technique for the treatment of generalized traumatic periodontitis of a chronic course.*
The study of supra (hyper) contacts and the presence of traumatic occlusion can support the initiation of chronic inflammation in the marginal periodontium against the background of a violation of the barrier function of epithelial attachment and a widespread violation of microcirculation. Local antibacterial treatment, professional hygiene of the oral cavity only temporarily relieves the symptoms of inflammation. In this regard, research is needed to determine the capabilities of autoimmune competent cells that have immunocorrelative abilities to support the local immune status in the periodontium. This is a brief review of the literature on the use of immunocompetent cells – platelets as key regulators of inflammation and immunoregulatory factors within vascular homeostasis to support local immune status. An up-to-date pathophysiological assessment of the use of PRF and i-PRF techniques, platelet growth factors for the creation of type I collagen, which plays a leading role in repair, is given. A current pathophysiological assessment of the stagnation of PRF and i-PRF techniques, platelet growth factors for the creation of type I collagen, which plays a leading role in repair, is given. It is appreciated that macrophages in the midst of inflammation play a special role in vibrating growth factors, such as platelet-derived growth factor (PDGF), transforming endothelial growth factor (TGF), which also mediates chemotaxis to stimulate angiogenesis. It was found that i-PRF can sense the functional differentiation of cells similar to osteoblasts, lower blood cells. The i-PRF culture infuses the production of primary human osteoblasts before proliferation, differentiation, mineralization of adhesion teams and migration. When administered regularly, PRF and i-PRF induce a three-fold increase in human osteoblasts and proliferation processes. A negative impact on cell vitality, metabolic activity and cell migration is prevented if the i-PRF concentration exceeds 60%. These studies concern a clinically significant topic related to the treatment of chronic periodontitis and obtained by non-surgical methods of regenerative processes in the periodontal complex, which is important for the clinical practice of dentists.

Key words: *traumatic periodontitis, platelet factors, PRF, i-PRF, VEGF, local immunity.*

Many works in the scientific literature are devoted to the issue of treatment of generalized periodontitis of the initial-first degree of the chronic course (GP). At the same time, complex treatment, which is based on etiotropic, pathogenetic and symptomatic, is quite multifaceted, and at the same time, it is not specified for individual treatment. This is due to the fact that the dominant factors that cause and support this inflammatory process in the alveolar processes differ in cases in terms of significance and causality. These are difficulties for the practical dentist. Carrying out only professional hygiene of the oral cavity, followed by daily use of means and methods of oral cavity care, patients do not always and do not fully solve the issue of treatment and stabilization of inflammatory processes in the periodontium. This is especially evident in young people aged 20-35, without detection of general somatic diseases with satisfactory immunogram indicators. In such situations, the question of the imbalance of indicators of the general and local immune response is not relevant. However, it should be noted that after carrying out local antibacterial and hygienic measures of the oral cavity by a dentist, the state of the phase of stabilization and remission of the disease is not always achieved. In this regard, a more detailed comprehensive local examination of patients aged 20-35 years with initial changes in periodontal tissues was conducted. Special attention was paid to the study of the state of super (hyper) contacts and the presence of traumatic nodes, traumatic occlusion, which can participate and support the initiation of chronic inflammation in the periodontium against the background of a violation of the barrier function of the epithelial attachment due to a widespread violation of microcirculation, changes in the endothelial system. as well as in alveolar processes. This concept of clinical manifestations is interpreted in the international systematization of periodontal diseases and peri-implantitis [4, 13] (2018, Amsterdam) as traumatic generalized marginal periodontitis.

Taking into account the tasks of treatment of this disease, where microcirculation disorders are the leading factors, followed by the elimination of local traumatic factors and antibacterial therapy, the stabilization of this process requires additional non-standard methods to achieve self-regulation of the process and remission of the disease.

This prompted a search for scientific literature on the use of factors for local regulation of chronic inflammation at the expense of one's own immunocompetent blood cells [19]. Why are platelet cells selected and the PRF, i-PRF technique used by dentists? The given short scientific review of the literature will allow us to highlight the main directions of platelet regulation mechanisms.

Recent studies show the fate of platelets as one of the key regulators in inflammation and intravascular immunity [11, 12, 16].

In addition to participating in the hemostasis system, platelets perform many other functions, including during inflammation. They contain a number of inflammatory peptides and protein mediators, some of which have the ability to be synthesized de novo, while others are stored and secreted from granules (α-granules, dense granules, lysosomes). These granules store many important platelet inflammatory and immune mediators, which are rapidly released after platelet activation, while the platelets increase in size, penetrate the foci of inflammation, and release significant amounts of proinflammatory substances from intracellular granules.

To date, numerous trials have been published, during which the inflammatory and regulatory potential of platelets has been investigated in detail. [14] It has been shown that platelets induce the secretion of biologically active substances and express a significant number of receptors, soluble molecules and signaling factors, which allow them to provide large-scale participation in the body's immune system. Although the first reports of platelet aggregation around bacteria date back more than 100 years, researchers have only recently begun to understand the complex interactions between platelets and innate immune cells in response to inflammation and infection [15]. Platelets can form complexes with neutrophils and increase their phagocytosis, produce ROS and NET formation, etc. As a result of interaction with blood cells, bacteria and viruses are removed from the immune system in various ways (both directly and indirectly) [17, 18].

Platelets are increasingly recognized as immune cells, as their role as a factor influencing the immune system has been established.

Growth factors play an important role in the multicomponent system of cellular regulation of body tissue repair processes. Growth factors are polypeptides with a molecular weight of 5-50 kDa, which are combined into a group of trophic regulatory substances. Being biologically active substances, they have a wide range of action – they stimulate or inhibit differentiation different cells and serve as the main carriers of the mitogenic signal. Growth factors were first discovered as a result of their ability to stimulate cell mitoses in serum-free culture in 1956 in the USA [3, 7].

In order for growth factors to exert a positive influence on the wound process, a critical minimum concentration of physiologically active cytokines in the wound is necessary. If growth factors are produced slowly or metabolized quickly, they will not perform their immediate functions. Growth factors are a kind of local stimulators of physiological processes, which also contribute to the neutralization of the inhibitory effect of various negative factors [6]. Platelet growth factor (PDGF) is one of the mitogenic polypeptides found in human blood. It is a thermally stable transmembrane glycoprotein, the specific feature of which is the extracellular N-terminal domain. There are three isoforms of transforming growth factor: AA-, BB- and AV- isoforms. They are formed depending on the placement of two chains A and B, which are connected by disulfide bonds and are the products of 4 different genes that belong to the PDGF/VEGF superfamily. All three isoforms differ both in terms of functionality and type of secretion [12, 18].

According to modern ideas, one of the main factors of angiogenesis is the platelet growth factor. The process of formation of new vessels is necessary for the adaptation of tissues in case of damage. One of the conditions for wound healing and the formation of a normotrophic scar is the growth of new capillaries to restore tissue oxygenation. Hypoxia and impaired microcirculation lead to the accumulation of decay products and inflammatory mediators, which contribute to the formation of a pathological scar. In the first 10 minutes after tissue damage, vasoconstriction of microvessels occurs in the wound, which leads to a gradual decrease in their tone and filling of the wound with blood. Platelet growth factor is released from platelets during blood clotting. All PDGF proteins are synthesized in an inactive proform, which undergoes intracellular proteolytic processing and turns into an active form. It is activated when platelets interact with thrombin, as a result of which PDGF is released into the blood serum and stimulates the proliferation of endothelial cells, creating conditions for the formation of new blood vessels and the formation of a capillary network of granulation tissue that fills the tissue defect. The release of platelet growth factor requires a strict dosage, limited to the maximum concentration and uniform distribution in the intercellular space, since pathological changes in the newly formed vessels may occur with an imbalance of its content. It can be an increase in their number, diameter, violation of permeability, etc [1, 2].

These provisions are of practical importance for understanding pathological processes in periodontal tissues, for determining the inflammatory phase and creating directed regeneration, during the treatment of patients with generalized periodontitis, especially in areas of excessive pressure on vessels.

Platelets directly recognize pathogens, activate and recruit leukocytes to the site of inflammation and infection, and modulate the behavior of leukocytes, increasing their ability to phagocytose, destroy pathogens, and stimulate unique effector functions, such as the production of neutrophil traps. At the same time, platelets participate in natural immunity, play a crucial role in innate and adaptive immune responses, and extensively interact with endothelial cells, various pathogens, and almost all known types of immune cells, including neutrophils, monocytes, macrophages, lymphocytes. In addition, platelets influence wound healing by integrating complex cascades between their mediators, which include various cytokines, transforming and platelet-derived growth factors, vascular endothelium. Recent evidence suggests that platelets play a significant role in the pathogenesis of malignant neoplasms, forming complex, bidirectional interactions with tumor cells.

Only part of the platelet population is required to maintain adequate hemostasis. Their excessive number allows these cells to play a role the first and main "circulating sentinels" to recognize foreign bodies, activating antimicrobial defenses, determining the presence of pathogens through their multiple immune receptors.

Platelet-enriched fibrin – PRF – is the most commonly used platelet concentrate in dentistry. Of particular importance recently is i-PRF – an injectable saturated platelet-rich fibrin, which has the properties of increasing vascularization and helps to accelerate wound healing. The advantage of i-PRF is that it shows the release of growth factors and promotes cell migration by announcing the expression of collagen type 1 and transforming growth factor mRNA, which affects osteoblasts, the connective tissue cells of the obligate ligament [6, 8-11].

Platelet-rich plasma (PRP) is used in regenerative dentistry as a supraphysiological concentrate of autologous growth factors capable of stimulating tissue regeneration. Despite this, concerns have been raised about the use of anticoagulants, agents known to inhibit wound healing. This study investigated a liquid formulation of platelet-rich fibrin (PRF), called injectable PRF (i-PRF), without the use of anticoagulants. Standard PRP and i-PRF (centrifuged at 700 rpm (60G) for 3 min) were compared for growth factor release up to 10 days (8 donor samples). In addition, the biocompatibility of fibroblasts after 24 hours (live/dead analysis); migration after

24 hours; examined proliferation on days 1, 3, and 5, and expression of PDGF, TGF-β, and collagen1 on days 3 and 7 [5].

Growth factor release demonstrated that overall PRP had a longer early period of growth factor release, while i-PRF demonstrated significantly higher levels of total sustained release of PDGF-AA, PDGF-AB, EGF, and IGF-1 at 10 days. PRP showed higher levels of TGF-β1 and VEGF after 10 days. Although both formulations showed high biocompatibility and higher fibroblast migration and proliferation compared to control tissue culture plastic, i-PRF induced significantly higher migration, while PRP showed significantly higher cell proliferation. In addition, i-PRF demonstrated significantly higher TGF-β mRNA levels at 7 days, PDGF at 3 days, and collagen1 expression at both 3 and 7 days compared to PRP. Conclusions: i-PRF demonstrated the ability to release higher concentrations of various growth factors and induced greater fibroblast migration and expression of PDGF, TGF-β, and collagen1. Future animal studies are now anticipated to confirm the use of i-PRF as a bioactive agent capable of stimulating tissue regeneration. Clinical Relevance: The results of this study demonstrate that a potent composition of liquid platelet concentrates can be obtained without the use of anticoagulants [5].

Thus, the analysis of the obtained literature data allows us to come to the conclusion about the need for an in-depth study of the use of platelet factors in the diagnosis of pathogenic changes in the periodontium in patients with generalized traumatic marginal periodontitis of a chronic course. In addition, determining the level of pro-inflammatory cytokines and vascular endothelial growth factor contributes to the practical and theoretical understanding of the prescription of therapeutic agents, primarily the use of the PRF, i-PRF technique in the treatment of patients with the specified dental status.

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