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Antioxidant Therapy in Complex Treatment of Parodontitis

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Abstract*: *Inflammatory periodontal diseases are one of the most pressing problems in dentistry. The paper presents a method of chronic generalized periodontitis treatment with the use of the antioxidant drug cytoflavin in combination with platelet gel, which is used as a dosing vehicle. Among the antioxidants, cytoflavin is one of the most interesting new Russian drugs. It has a complex effect on the body with a pronounced clinical effect. The advantages of using platelet gel are safety (no risk of infectious diseases or the occurrence of immunogenic reactions), the non-invasiveness of the procedure itself, the delivery of growth factors and cytokines directly to the wound area, and the speed and simplicity of the platelet gel preparation.

Index Terms*: *cytoflain, platelet gel, periodontium, antioxidants, hypoxia, platelet activation, dentistry, tissue regeneration.

I. INTRODUCTION

Inflammatory periodontal diseases are one of the most pressing problems in dentistry. They have social significance because they are widespread, cause severe changes in the periodontal tissues and in the entire patient's body, and affect young people. Periods of remission and exacerbation occur during the course of inflammatory diseases of periodontal tissues, which often significantly disrupt the function of the dental system due to bone resorption and damage of the dental apparatus [1].The most important task of a medical practitioner is to preserve the health and well-being of the patient. In dentistry, this means, first of all, the prevention of diseases of the oral cavity. If despite ongoing preventive treatment, destruction of the teeth and periodontal tissues occurs, periodontal treatment becomes the foundation upon which further dental treatment is based. Any restoration, from a small filling to complex dental bridgework on implants, can be performed only when the supporting periodontal structures are healthy and not inflamed [2, 3]. In the pathogenesis of generalized periodontitis, it is important to consider disruptions of the trophism (metabolism and morphology) of periodontium associated with the deterioration of microcirculation of functional and organic nature, imbalance of nervous and hormonal regulation, immunocompetent and barrier systems [4, 5]. As a result, periodontal hypoxia occurs, leading to the activation of free radical oxidation processes. Activation of free radical oxidation can be considered as the adaptation mechanism of the organism to changes in the oxygen levels in the tissues. The result of free radical oxidation is the formation of reactive oxygen intermediates (superoxide anion, hydroxyl radical). Normally, the generation of reactive oxygen intermediates in tissues induces the synthesis of protective systems: antioxidants and other protective substances. However, with age and due to various precipitating causes, the antioxidant defense system becomes unable to react adequately and synthesize a sufficient amount of antioxidant complexes. As a result, an imbalance occurs in the free radical oxidation/antioxidant protection system with a shift towards the first. When antioxidant protection fails, free radical oxidation in the periodontium develops as an avalanche. The level of peroxidation of cell membrane phospholipids increases, membranes disintegrate, and periodontal cells die with the release of endogenous toxins. Cell division is disrupted and inert products of lipid and protein peroxidation accumulate [6, 7]. Activation of free radical oxidation in the epithelial layer and deeper periodontal structures can be one of the factors that inhibit the resistance of the latter to adverse impacts, which creates conditions for the practically unhindered spread of the inflammatory process.In the case of periodontitis, the activity of superoxide dismutase in the gum is reduced. The activity of catalase, glutathione peroxidase, cytochrome oxidase is also often reduced. However, the level of sulfhydryl groups is increased, which indicates the disintegration of proteins. A statistically significant correlation has been established between the content of free radical oxidation products in the gum fluid and the depth of the periodontal pockets. The content of malondialdehyde in the gum blood increases in proportion with the severity of the disease, which also indicates the activation of free radical oxidation during periodontitis and can serve as substantiation for antioxidant therapy [5, 8, 9]. Among the antioxidants, cytoflavin is one of the most interesting new Russian drugs. It has a complex effect on the body with a pronounced clinical effect. Our analysis of the available literature showed no data on the active use of cytoflavin for the treatment of chronic generalized periodontitis. The pharmacological effect is associated with the complex effect of the cytoflavin formula components. 1 ml of cytoflavin solution contains succinic acid – 100 mg, nicotinamide – 10 mg, Riboxinum (inosine) – 20 mg, riboflavin mononucleotide (riboflavin) – 2 mg, excipients: N-methylglucamine – 165 mg, sodium hydroxide – 34 mg, water for injections.

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The substantiation for the use of cytoflavin in the treatment of chronic generalized periodontitis is its ability to stimulate respiration and energy production in cells, improve oxygen utilization by tissues, restore the activity of antioxidant protection enzymes, and activate intracellular protein synthesis. Another significant problem is the delivery method of cytoflavin for the local administration. This drug is available in the dosage forms of pills and solution for injection, which makes it difficult to deliver it to the periodontal pockets. To solve this problem, we propose the use of cytoflavin together with platelet gel (PG). PG is one of the latest advances in dentistry and is used to improve the healing process of soft and hard tissues after surgery. It also accelerates the processes of healing and recovery in cases of obstinate generalized aggressive periodontitis, reconstructive oral and maxillofacial surgery, surgical repair of alveolar clefts, oral-antral and oral-nasal fistulas, and installation of bone-integrated implants [10]. PG has been shown to effectively accelerate the healing of soft tissues and epithelialization after transplantation of free connective tissue grafts, manipulations with mucoperiosteal flaps, and soft tissue buildup during cosmetic interventions in the oral cavity.

PG contains three to five times more platelets than normal blood (up to one million platelets in 1 µl of blood plasma), which increases the concentration of natural growth factors produced by platelets, stimulates local angiogenesis, attracts pluripotent stem cells to the damaged area, and starts the division of cells involved in the process of tissue regeneration. Platelet-rich plasma contains platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), epithelial growth factor (EGF), and adhesion molecules (fibrin, fibronectin, vitronectin). The fibrin component of the PG facilitates the binding of particles of bone material and promotes osteoconduction through the formation of a network that acts as a skeleton and supports the growth of new bone. The combination of these factors can reduce the time of growth and maturation of bone tissue. The advantages of using PG are safety (no risk of infectious diseases or the occurrence of immunogenic reactions), the non-invasiveness of the procedure itself, the delivery of growth factors and cytokines directly to the wound area, and the speed and simplicity of the PG preparation. To obtain the PG, 45-60 ml of blood is taken from a patient immediately before the operation into a syringe containing anticoagulant based on citrate and dextrose. Blood is fractionated using double centrifugation. Erythrocytes are separated from leukocytes, platelets, and platelet-poor plasma during the first cycle of centrifugation at low speed. At this stage, a plasma preparation with a low platelet concentration is obtained. To obtain a platelet concentrate, repeated centrifugation of the plasma fraction is required. Platelet-rich plasma is kept sterile in a liquid state for eight hours, so it can be used for prolonged surgical interventions. Platelets are activated by mixing 7 ml of platelet concentrate with 1 ml of a mixture containing 5,000 UE of topical bovine thrombin and 10% of calcium chloride solution, as well as 1 ml of air and 750 mg of cytoflavin powder (maximum dose per one ingestion of the drug). After shaking for ten seconds, the material acquires the consistency of a viscous gel. During the first ten minutes, platelets secrete about 70% of the growth factors they contain, and their complete release occurs within an hour. PG retains activity for about 8 days, after that period platelets die. The use of PG accelerates the healing of soft tissues and contributes to the rapid mineralization of new emerging bone. The drug component of the medicinal preparation has an effect within 12 hours [11].

II. MATERIALS AND METHODS

The study was supported by the "Project for the competitiveness of leading Russian universities among the world's leading research and educational centers". We observed 80 patients aged 18-65 years with chronic generalized periodontitis: 26 had mild, 40 – moderate, and 14 – severe periodontitis. We divided patients into three groups: 27 patients in the first group received traditional treatment, 26 patients in the second group received cytoflavin in the form of applications in addition to traditional treatment, 27 patients in the third group received combined treatment with the use of traditional methods and the cytoflavin/PG complex. The gel we obtained had a doughy texture and was modeled into patches, the dimensions of which allowed to install them into the periodontal pockets. Patients were re-examined after one month. Traditional treatment included hygiene training and professional hygiene (removal of supra- and subgingival dental plaque, polishing of the teeth surfaces). Depending on the depth of the periodontal pockets, appropriate surgical treatment (curettage, open curettage) and, if necessary, removal of teeth, the preservation of which became impossible, was performed. Preoperative preparation of periodontitis patients included dental treatment and the replacement of low-quality fillings. Local anti-inflammatory medicinal treatment included washing of periodontal pockets with a 0.06% chlorhexidine digluconate solution. We started surgical treatment when the level of individual hygiene of the oral cavity met the highest criterion according to the index score. During the postoperative period, nonsteroidal anti-inflammatory drugs, desensitizing, and antibacterial therapy were prescribed. Chlorhexidine solution was used locally for rinsing.

III. RESULTS AND DISCUSSION

Among the 27 patients from the first group: eleven had mild generalized chronic periodontitis; 11 had moderately severe chronic generalized periodontitis, and five had severe chronic generalized periodontitis. Improvement of dental status and positive dynamics of the periodontal index (PI) were observed in these patients after traditional treatment. We observed a decrease in teeth mobility, induration of the gingival margin, and reduction (in several cases – disappearance) of periodontal pockets in patients with mild and moderate severity. PI decreased from 4.23 ± 0.08 to 1.83 ± 0.04. Among the 26 patients from the second group, in which applications with a solution of cytoflavin in 10 ml of water for injection were used in addition to the traditional treatment: eight had mild generalized chronic periodontitis; 14 had moderately severe chronic generalized periodontitis, and four had severe chronic generalized periodontitis.

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One month after the treatment, induration of the gingival margin and reduction of periodontal pockets was observed. PI decreased from 4.23 ± 0.08 to 1.25 ± 0.04. The results of complex treatment of chronic generalized periodontitis in 27 patients with the use of periodontal dressings with the cytoflavin/PG complex after one month allowed us to establish a significant improvement in dental status. PI decreased to 0.45 ± 0.04. Orthopantomograms after three and six months after the treatment demonstrated that the condition of the bone tissue of the alveolar processes stabilized.

IV. CONCLUSION

The treatment of chronic generalized periodontitis with the use of cytoflavin in combination with PG is innovative and has shown high efficiency compared with the traditional method of treatment. Analysis of the data of clinical and radiological studies allows us to conclude that the use of this method is viable, promising and requires further research. The preparation of the cytoflavin/PG complex is not difficult and can be carried out within the dental clinic, which makes possible the active use of this method by dentists.

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