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COMPLEX TREATMENT OF PATIENTS WITH THE USE OF IMMUNOCORRECTIVE THERAPY IN PATIENTS WITH RAPIDLY PROGRESSIVE PERIODONTITIS

Jabbarova Zarnigor
Assistant of orthopedic dentistry, 5th year student of the Faculty of Dentistry, Samarkand State Medical University, Uzbekistan

Axmadov Farrux
Assistant of orthopedic dentistry, 5th year student of the Faculty of Dentistry, Samarkand State Medical University, Uzbekistan

Kudratova Nozanin
Assistant of orthopedic dentistry, 5th year student of the Faculty of Dentistry, Samarkand State Medical University, Uzbekistan

ABOUT ARTICLE

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Abstract: Periodontal diseases are a serious problem of modern medicine due to their almost 100% prevalence and increasing incidence among young people. At the same time, aggressive forms are increasingly common, especially rapidly progressive periodontitis (BPP), the course of which repeats almost continuously. Prevention and improvement of the effectiveness of complex treatment of periodontal diseases, especially rapidly progressive periodontitis, has become an urgent problem of modern dentistry.

INTRODUCTION

Periodontal diseases are a serious problem of modern medicine due to their almost 100% prevalence and increasing incidence among young people [1]. At the same time, aggressive forms are increasingly common, especially rapidly progressive periodontitis (BPP), the course of which repeats almost continuously.[2] Prevention and improvement of the effectiveness of complex treatment of periodontal diseases, especially rapidly progressive periodontitis, has become an urgent problem of modern dentistry. The atypical nature of rapidly progressing periodontitis is manifested in the fact that the active destruction of the supporting tissues of the tooth begins at a young

age of 20-25 years. The disease progresses with violent clinical manifestations and is accompanied by a very rapid and massive loss of all periodontal tissues, mainly the jawbone, which practically cannot be treated with traditional means, and in a relatively short period of time (5-7 years) leads to complete loss of teeth, as a result of which has a very unfavorable prognosis [3]. According to many authors, the main etiology in the development of atypical forms of inflammatory periodontal diseases, especially DPP, is Actinobacillus actinomycetem comitans, Prevotella intermedia, Porphyromonas gingivalis, which is part of plaque and is characterized by the greatest aggressiveness and ability to penetrate periodontal tissues [4,5]. These microorganisms are involved in the formation of the body's immune response to the introduction of periodontal tissue, causing the development of autoimmune inflammation or immunodeficiency [6, 7]. Currently, the important role of occupational and anti-inflammatory cytokines in the regulation of inflammation in periodontal tissues has been established. An increase in the production of antigen-stimulating monocytes, tissue macrophages, lymphoid tissues (IL-1, IL-6, IL-8 and many others) of inflammatory cytokines is accompanied by the development of polymodal local and long-term effects, which ultimately lead to microcirculation disorders in periodontal tissues, degradation of collagen in periodontal ligaments, bone resorption of alveolar processes of the jaw due to indirect differentiation of osteoclast precursors [8]. Transforming growth factor TGF-β1 has an inhibitory effect on the synthesis of inflammatory cytokines, stimulates fibroblast proliferation, synthesis of intercellular matrix proteins, collagen and, ultimately, regeneration processes. Recently, a new element of tumor necrosis factor osteoproteinin has been identified, a protein synthesized by osteoblasts, an important link that inhibits the differentiation and activation of osteoclasts and, therefore, is very important in the process of bone resorption [8]. Osteoprotegerin inhibits the binding of rank and rank ligands, thereby inhibiting the mobilization, proliferation and activation of osteoclasts. The stimulating and inhibitory effect of cytokines is carried out by binding them to a large number of receptors on the cell surface, leading to inflammation, regeneration and development of immune reactions for these reasons, pathogenetically justified in the complex treatment of periodontal diseases, an essential component is immunocorrective therapy, which is aimed at activating local immunity, that is, increasing the ability of tissues to protect themselves as effectively as possible from infection, [9] It is possible to stimulate the immune system to stimulate the immune system. The search for new immunological drugs allowed us to pay attention to the drug gepon, which not only has immunomodulatory properties by changing the spectrum of cytokines synthesized by cells, but also increases the functional activity of fibroblasts and epithelial cells and improves the regenerative ability of periodontal tissues. The purpose of the study: to increase the effectiveness of complex treatment of patients with rapidly progressive periodontitis by using the drug gepon.

METHOD

A survey of 80 people was conducted, which included 20 practically healthy volunteers and 60 patients with STD. All patients were divided into 2 groups: group I (30 people) consisted of patients with BPP who received complex treatment using the immunocorrective drug gepon, and in group II (30 people) criteria for inclusion of patients in traditional studies: age from 17 to 35 years; reliable diagnosis of BPP, informed consent of the patient. When collecting anamnesis in all patients, factors such as the duration of the disease, the nature of the periodontal process, the results of previous treatment and the duration of remission were taken into account. To monitor patients and objectively assess the condition of periodontal tissues during treatment, simplified hygienic indicators, indicators of bleeding gums, papillary-limbic-alveolar indices, periodontal indices, determination of pathological tooth mobility, determination of the depth of periodontal pockets were used. An X—ray examination of the dental system was performed - orthopentomograms and targeted intraoral radiography of individual groups of teeth [10]. Immunological examination: The study of cytokines (IL-1β, IL-8, IFN-u, IL-4, IL-10), transforming growth factor β and BPP in patients in the exudate of periodontal pockets by solid-phase enzyme immunoassay using vector best reagents is carried out at the first visit before starting treatment, 1 month after a course of local therapy for preoperative preparation, 3 months after surgical treatment and 6 months after the start of treatment in the long term. "I won't let that happen." All patients received comprehensive treatment, including: control and correction of individual oral hygiene; professional oral hygiene (removal of dental deposits on upper teeth and subgingival teeth) followed by drug irrigation of periodontal pockets with 0.06% chlorhexidine bigluconate solution; elimination of local factors contributing to the accumulation and activation of microbial factors (filling of the gum cavity, removal of defective fillings, restoration of interdental contact); Inorganic matrix - splints of movable teeth using fiberglass-based materials (GlasSpan, USA, and Fiber Splint, Switzerland) and liquid photopolymers; functional selective grinding, alignment of the occlusal surface to eliminate traumatic nodes, according to indications, correction of soft tissues of the vestibule of the oral cavity was performed. The complex of preoperative preparation of group I patients included the drug gepon (Immafarma), which belongs to the group of immunomodulators. Gepon is a synthetic peptide consisting of 2 mg, 14 amino acid residues each, dissolved in vials in 2 ml of water for injection. The dentition was separated from the saliva using an adsorption roller, and a periodontal pocket was applied to the gum by instillation. To determine the optimal method of using the drug in a group of patients (15 people), gepon was used in the form of ointment (gepon0.006; lanolin 10.0; olive oil 10.0; water for injection 10.0). The course of treatment consisted of 1 procedure, which was performed every 10 days. General treatment included administration of the antimicrobial drug Rulid 150 mg 2 times a

day in the pre- and postoperative period 1-2 times a day, 200 mg 1 time a day in combination with nizoral for 10-14 days (depending on clinical dynamics). Statistical processing of cytokine results was performed using a series of Stat Soft Statistica v6.0 programs. The results were presented as a median in the interquartile range (25-75 percentiles), and the Kruskal—Wallis criterion was used to determine the reliability of differences between groups. Results. In patients with rapidly progressive periodontitis, according to the medical history, the duration of the disease ranged from 1 to 5 years. During the examination of the patient, complaints of bad breath, hyperemia of the gum area, bleeding when brushing teeth, when eating solid food, the presence of dental deposits, changes in the position and mobility of teeth, as well as regular suppuration were revealed. An objective examination revealed inflammatory phenomena, swelling of the gingival papilla, gum hyperemia and severe bleeding. The value of the PMA index was 47.75 ± 2.4 %; the depth of the periodontal pocket was 8.5 mm, PI-6.47 ± 0.05, tooth mobility was 2-3 degrees. Dental deposits were found on and under the gums in all patients. The UIG index was 2.2±0.05, which corresponded to poor oral hygiene. Orthopentomograms showed the disappearance of the compact plate, resorption of the alveolar gap by more than 1/2 of its height, vertical lesions of 4-8 mm in size (subclass B), pronounced destruction of the bone tissue of the interdental septum, characterized by a pronounced phenomenon of osteoporosis. In 19 (31.6%) patients with BPP, there was a difference between the severity of clinical manifestations and the degree of destructive processes of the bone tissue of the alveolar process of the jaw: radiologically, there was pronounced active destruction of bone tissue with minor inflammation of the gingival margin. In BPP, we found a noticeable cytokine imbalance in the exudate of the periodontal pocket. In all patients with BPP, the concentration of proinflammatory interleukin-1β increased almost 4 times compared with the data of the control group. The increase in IL-1ß content correlated with the depth of periodontal pockets (gIL-1b=0.512) and the degree of bleeding gums (gIL-1b=0.504). Therefore, the content of this cytokine in the exudate of the periodontal pocket can be considered an additional laboratory criterion for the severity of BPP. Interleukin-8 is the most important mediator of the inflammatory process produced by activated macrophages. In patients with BPH, the IL-8 content increased by more than 3 times compared to the control group. The immunomodulatory cytokine IFN-u was significantly reduced in the periodontal pocket exudate compared to the control values. This fact, in our opinion, is a sign of a serious violation of the local immunity of periodontal complex tissues in patients with bpp, which steadily finds its manifestations in progressive inflammatory and destructive processes and the torpedo course of the disease. The state of oral immunity is largely determined by the optimal level of anti-inflammatory interleukin-2, which inhibits the activation of macrophages and produces T lymphocytes of the Th-4 subpopulation. In BPP, the development of local immune reactions is observed mainly along

the Th2 pathway. Our study shows that in the exudate of periodontal pockets in patients with bpp, the content of interleukin-4 was significantly reduced to 4.81±1.81 pg/ml and 3.49±2.1pg/ml compared with 13.51±1.21 in the control group. The content of anti-inflammatory IL-10 in patients with BPP before treatment also decreased by 1.7 times compared to the control values. The most important mediator involved in the proliferation and differentiation of lymphocytes and, ultimately, in the regeneration of periodontal tissues is the transforming growth factor TGF-β1. The content of TGF-β1 in patients with BPH is 2.4 times higher than the control value. At the same time, in 9 (15%) patients, the value of this indicator, on the contrary, decreased. TGF-β1 is involved in tissue remodeling, and the long-term recurrent course of the disease leads to disruption of the processes of reepithelization and regeneration, weakening of the intercellular matrix, excessive migration of fibroblasts to the affected area with the development of fibrosis. Another indicator that allows you to indirectly assess the condition of bone tissue is osteoprotegerin—OPG, the value of which in patients with bpp was also lower than in the control group. A 2.5-fold decrease in OPG level creates conditions for the activation of bone macrophages and promotes progressive bone resorption of the alveolar processes of the jaw. Analyzing the results obtained, it should be emphasized that the cytokine network is a sensitive, balanced regulatory network. A comparison of the concentrations of pro-inflammatory and anti-inflammatory cytokines in patients with BPH revealed a noticeable imbalance in their ratios compared with the ratio of control values. Thus, if in a healthy donor the ratio of IL-1β/IL-4 content in the gingival fluid was 8.61±0.93, then in BPP this ratio increased due to an increase in IL-1β to 13.08±1.04. 1β, IL-8), effects of TGF-β1, superantigen, proliferation of pathogenic paradont flora and depletion of IFN-γ and OPG in the periodontal pocket, mediated by a decrease in the level of anti-inflammatory cytokines (IL-4, IL-10), are based on significant changes in local immunity. The use of the immunocortical drug gepon in the complex preoperative preparation of patients with BPP allowed, after 1 month of follow-up, to reduce the level of inflammatory cytokines IL-1β, IL-8 in the contents of the periodontal pocket by 3.3 and 2.5 times, respectively. This dynamics persists for 3 months of follow-up, and the content of IL-1β, IL-8 is 3.5 and 2.6 times lower than the initial value. The amount of IFN-γ and OPG in the PC contents increased 2.5 times and 2.4 times after 1 month, respectively, and after 3 months the value did not change significantly. Otherwise, there is a situation with the content of cytokines of anti-inflammatory action. After 1 month of follow-up, a significant ($p \geq 0.001$) increase in IL-4 and IL-10 levels was found to be 1.7 and 1.5 times, respectively. The received value is saved after 3 months. The concentration of TGF-β1 in the PC contents of patients with BPP gradually changed, and after 1 month it decreased slightly by 1.3 times, and after 3 months it decreased even more by 2.2 times. This situation may indicate the activation of regenerative processes in periodontal tissues, which are clearly present

after complex treatment, including modern and effective immunocorrective drugs and high-quality surgical treatment. In group II, local treatment of bpp was carried out without the use of immunocorrective agents. After 1 month of follow-up, the concentration of inflammatory cytokines IL-1β, IL-8 in the PC content significantly decreased by 1.3 and 1.6 times, respectively ($p \geq 0.001$), the content of anti-inflammatory cytokines IFN-γ increased slightly by 1.3 times, and the concentration of OPG in the PC content did not significantly change after 1 month. The concentration of TGF-β1 in the PC content in patients with BPP decreased slightly after 1 month. At the same time, after 3 months, the cytokine concentration does not have a statistically significant difference from the indicators before treatment and, together with the clinical picture, indicates a low effectiveness of treatment for BPP without the use of immunocorrective therapy. Discussion. Analyzing the results obtained, it could be concluded that the complex treatment of patients with rapidly progressive periodontitis using a course of gepon provides normalization of the cytokine balance, manifested in a decrease in the level of inflammatory cytokines, an increase in the level of anti-inflammatory interleukins. At the same time, there is a significant improvement in the indicator of the main immunomodulatory mediator IFN-γ.The transformation of the growth factor TGF-β1 and an increase in the content of osteoproteinin indirectly confirm the improvement of the bone tissue of the alveolar processes of the jaw. When examining patients with BPP after 1 month of gepon use as part of complex treatment, in 71% of patients, the sbi and PMA bleeding index approached normal values. In 29% of patients, signs of gingival margin inflammation were observed, while in 17% of patients, the value of the SBI index exceeded 15%. In the comparison group (II), after 1 month, the value of the sbi and PMA bleeding index approaches zero in only 10% of patients, and at the same time, 90% of patients retain signs of periodontal tissue inflammation, this is due to, that the analysis of the clinical effectiveness of complex preoperative preparation of patients with BPP according to the SBI index significantly good results are achieved when using gepon with an anti-inflammatory effect by 1.5 times, conduct a comparative assessment of dynamic changes in clinical parameters at the stage of complex treatment of patients with BPP using gepon in the form of ointment, make sure of the advantages of using gepon in the form of ointment Gepon ointment is easily applied and it does not spread, this is especially important when applied to the upper jaw, it is fixed in the periodontal pocket and the gum mucosa, the optimal concentration of the drug is maintained for a longer time, it can also be used to cover the bandage (Septopack). In the group of patients treated with Gepon ointment, the best dynamics of attenuation of inflammatory processes in periodontal tissues (SBI and PMA bleeding index) is on average 2-4 days, and when examining patients with BPP after 3 months of surgical treatment, clinical remission is observed in 78% of patients in group I, and 51% are in the comparison group. However, after 6 months of follow-up,

there was a clear increase in the PMA index in the group of patients treated with traditional methods. The data obtained allow us to conclude that the use of gepon in the complex treatment of BPP using basic anti-inflammatory therapy allows to achieve stable remission in 6% and 56% of patients after 71 months, and the bone suppressant Bio-Oss (Geistlich, Switzerland) and the absorbable two-layer collagen membrane Bio-Gide (Geistlich, Switzerland). (Used at the stage of surgical treatment), Ramfjord flap surgery performed an operation using a bone conduction flap with complete detachment of the flap and filling of the bone pocket.drugs. . Surgical treatment was performed immediately after immunomodulatory therapy. At the stage of surgical treatment, Ramfjord flap surgery was used, for which 3 horizontal incisions were made: toothed, retreating 0.5-1 mm from the gingival margin, repeating the contour of the gum at an angle of 35 degrees to the tooth, adjacent to the incisions around each tooth and the incisions between the teeth in the longitudinal direction under the gum papilla. These incisions create a remodeling of the gingival margin, and the delicate condition of the inner surface of the flap is preserved without significant damage to the periosteum. Thorough curettage was performed, all affected granulation tissues, subgingival deposits of the tooth and altered root cement were carefully sanded and polished for removal, and blood was taken from the patient's ulnar vein using EMS ultrasound into a sterile vacuum tube in an amount of 15-20 ml and centrifuged. Bio-OSS was impregnated with platelet-rich plasma and placed in bone defects until the defect was completely visually closed. Next, a two-layer resorption collagen membrane was installed on both sides of the bone defect, before which it was given the desired shape with sterile scissors. Then they were sutured in the area of the interdental cavity and behind the dentition until the flap of the periosteum mucosa was firmly fixed. The use of the biogid membrane makes it possible to exclude the penetration of epithelium and connective tissue elements of the gum into the periodontal defect zone, as well as to form a space between the inner surface of the membrane and the affected surface of the root, a new cement of the tooth root is formed, and an osteoid matrix appears. The use of membranes contributes to the rapid organization of blood clots with the help of cellular and fibrous structures, the formation of collateral circulation, which creates all conditions for directed regeneration. The use of Bio-Gide membranes is aimed at creating a gum framework that separates bone tissue and prevents gum retraction and the formation of new periodontal pockets. Observations of patients receiving complex treatment using the immunomodulatory agent "gepon" showed that already on the 3rd-5th day after the start of treatment, a pronounced anti-inflammatory effect was observed. Gum bleeding decreases, self-confidence appears when chewing with teeth, a state of comfort in the oral cavity, the gingival margin thickens, and the general condition improves. After 2-3 weeks, with pronounced resorption of bone tissue and alveolar processes after immunomodulatory therapy and surgical treatment, there was a significant decrease in

the mobility of pathological teeth in the area of stabilization of the process and surgical intervention. This made it possible to preserve and strengthen movable teeth as much as possible, and then use them as supports for various types of dentures at the stage of orthopedic treatment. After 6 months of follow-up, the state of remission was clinically established. The process of bone formation was noted radiologically.

CONCLUSION

Summarizing the results of the study, it can be summarized that the local use of gepon at the stage of complex preoperative preparation for the correction of immune disorders and improvement of regeneration of the gingival epithelium in BPP provides greater effectiveness of surgical treatment: the duration of healing is 7.1 ± 1.6 days, and 5% of patients experienced complications in the postoperative period.In the group with traditional treatment, the duration of healing was 10.3 ±1.8 days (10% of complications). Due to the progressive course of the disease and the instability of the results obtained in some patients, it is recommended to repeat the course of immunocortical therapy with gepon 6 months after the surgical stage.

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