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Research Article

**INFLUENCE OF LASER TECHNIQUES ON THE WOUND
HEALING PROCESS IN THE AREA OF MUCOSA OF ORAL
CAVITY**Tarasenko S.V.¹, Gutorova A.M.², Diachkova E.Yu.³¹ M.D., PhD., Professor, Chief of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: prof_Tarasenko@rambler.ru² Postgraduate Student of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: anechka111108@mail.ru³ PhD, Associate Professor of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: secu2003@mail.ru, Phone Cell Number: +7-926-519-93-42**Abstract:**

It follows from the literature that an important component of clinical success in surgical dentistry is a favorable course of the wound process, the basis of which is regeneration. At the present level of development of surgical dentistry is not enough subjective characteristics in determining the clinical effectiveness of various methods. Objectively, the way of the wound healing process reflects the biochemical and immunological markers of regeneration and mediators of inflammation of the oral fluid. Data on a comprehensive study of the immunological reactivity of the body, the comparison of changes in its performance in various forms of inflammatory processes are virtually absent.

Currently, various devices in their technique and modes of laser radiation are used, while methodological information on the use of its in surgical dentistry is not enough. This has a negative impact on the frequency, effectiveness and safety of laser radiation, which causes reasonable uncertainty in practical dentists who do not have the appropriate conditions for the development of optimal techniques in practice. At the same time, the use of surgical lasers contributes to the economic and social effect. The urgency of the problem of comparative analysis of reparative processes depending on the method of surgical treatment and the need for further research expanding the practical use of modern, high-tech operations, with rapid rehabilitation of patients, reducing the number of complications, improving the results of treatment and cosmetic effect.

In our article we tried in short form to analyze the main factors of the wound healing and ways of decrease of postoperative inflammation using different kinds of laser radiation

Key words: *wound healing, mucosa, oral cavity, laser radiation, interleukin, immunoglobulins*

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INTRODUCTION:

Tissue regeneration is adjustable, multicomponent cascade of morphological and functional process that ensures the interactions of the cellular elements, many humoral factors and microflora. Biological laws are the same for healing wounds of any origin, the difference lies in the severity of complications and the timing of healing. The accumulated knowledge of clinical and immunological characteristics of the wound process, indicate that a key component of tissue regeneration is the regulation of humoral factors. The study of the pathomorphological and pathophysiological mechanisms is necessary to improve the diagnosis and surgical treatment of dental diseases [1].

I.Immunological aspects of the wound healing process

The way of the wound process is divided into three phases: 1) the phase of inflammation, consisting of 3 consecutive periods: 1) vascular changes and wound cleansing by suppressing the microflora and rejection (resorption) of non - viable tissues; 2) the regeneration phase: filling the wound with granulation tissue; 3) the phase of scar formation and reorganization (phase of the active epithelialization) [2].

The perspective of optimization of the wound process is the regulating influence on the balance between surgical alteration, stimulation of regeneration and control of inflammation. The launch of the cytokine cascade, including pro-inflammatory and anti-inflammatory mediators, the balance between the opposing groups of humoral factors determines the regulatory and functional immune disorders observed in surgical patients, the probability of transition of the local inflammatory process to generalized form, the development of purulent-inflammatory complications and, ultimately, the outcome of the disease [3].

Reparative regeneration is a genetically determined stereotypical process, but different tissues and organs differ significantly from each other in the degree of scar development. Numerous experimental and clinical studies have shown that compared with the skin, the healing of mucous membrane wounds occurs much faster and with less scar tissue formation [4,5,6]. The establishment of the reasons for this can contribute the development of new methods to control the way of reparative regeneration processes in various parts of the body, including the maxillofacial region [7].

The severity of scar tissue in postoperative wounds on the mucosa is depended on the immunological

tolerance in inflammatory processes, composition of growth factors [8], local phenotype of fibroblasts, the composition of the extracellular matrix and activity of apoptosis [9]. Without diminishing the importance of these factors in the process of scar tissue formation it should be noted that the ultrastructural characteristics of cellular and fibrillar structures at various stages of wound healing of the oral mucosa have not yet been clarified.

Negative conditions of regeneration of surgical wounds in the oral cavity are known: colonization of conditionally pathogenic microflora, mechanical and thermal load on tissues, specificity of histological structure. Almost all identified bacteria of the oral cavity can cause purulent-inflammatory processes. A wound complication in dental surgery is initiated primarily by virulent periodontopathogenic species of microorganisms. The microbial factor is one of the most significant during the wound process [10]. In this case, only the effects of microorganisms are not enough, the premorbid features of the patient's reactivity are important.

The development of inflammatory wound complications is determined by the state of cytokine regulation of the interaction of macro - and microorganisms. It is known that more than 90 % of bacteria exist in ecosystems not as separate plankton cells, but as biofilms attached to the substrate [11]. The process of interaction of periodontal pathogens of biofilm with toll-like receptors (TLR) of cells is significantly different from that involving normal microflora. Representatives of normal microflora, in contrast to pathogens, induce the formation of cytokine TFR β 1 (transforming growth factor β 1), which in turn inhibits the expression of TLR. It is important to identify preclinical signs of inflammatory and destructive process. Pro-inflammatory cytokines (IL-1 β , TNF, IL-6, IL-8) recruit the effector cells (neutrophils, macrophages) into the focus of inflammation, stimulate their phagocytic and bactericidal activity and induce the launch of an antigen-specific immune response [12].

The protectorate of proinflammatory cytokines is manifested in their presence in the focus of inflammation, but excessive and generalized production of proinflammatory cytokines leads to the development of organ dysfunction. To avoid excessive manifestations of the inflammatory process, the mechanism of negative feedback in the body includes control mechanisms mediated by the production of anti-inflammatory cytokines and soluble inhibitors of pro-inflammatory cytokines. A permanent character has the production of the

receptor antagonist IL-1 β (interleukin), competitive limiting activation of the cells under the influence of IL-1 β and at the same time exhibiting anti-inflammatory activity [13].

Protonic research method of mass spectrometry of the biofilm composition of the oral mucosa has found that the majority of biomarkers for infectious and inflammatory diseases of periodontium are breakdown products of connective and bone tissue [14]. The cell walls of pathogenic bacteria are a source of lipopolysaccharides interacting via toll-like receptors with damaged epithelium cells, neutrophilic granulocytes, monocytes/macrophages, fibroblasts [15]. Lipopolysaccharides of the cell wall of pathogenic bacteria stimulate neutrophils and macrophages to produce IL-1 β , which increases the rate of its production by autocrine mechanism. Leukotoxin of Actinomycetes triggers the secretion of active IL1 β by macrophages. With a constant massive flow of microbial agents the cytokine production becomes excessive. IL-1 β stimulates the production of matrix metalloproteinases, reduces the production of tissue inhibitor metalloproteinases, induces the synthesis of RANCL (a membrane protein, a cytokine of a family of tumor necrosis factors).

One of the factors of inflammation progression is activation of cytokine production and secretion. Activated monocytes and tissue macrophages synthesize both pro-inflammatory (IL-1 β , TNF, IL-6, IL-8) and anti-inflammatory cytokines (IL-10, TGF β). Changes in the cytokine profile of saliva in various diseases is an important diagnostic indicator of inflammation, immunoglobulins (IgA, IgM, IgG) secretory, as well as pro-inflammatory (IL-1 β , IL-6, IL-8, TNF) and anti-inflammatory (RAIL, IL-4, IL-10) cytokines are quantitatively determined by enzyme immunoassay. The predominance of pro- or anti-inflammatory cytokines leads to a decrease in the effectiveness of inflammation, the development of purulent complications or autoimmune pathology [16].

In the blood serum of patients with chronic generalized periodontitis the level of autoantibodies to IL-1 β , IL -8, IIL10 is much higher than in healthy individuals. Similar pattern was revealed in the study of the level of AAT in oral and gingival fluids. The forming antibodies eliminate the pro-inflammatory cytokines and prevent their penetration through hematosalivary barrier into the general circulation, thereby blocking the generalization of the inflammatory process. It is possible that among the autoantibodies detected by ELISA, can be enzyme

catalyzing peptidases.

With the predominance of pathogenic microflora through toll-like receptors a continuous flow of signals activating macrophages and other immunocompetent cells carrying these receptors is provided and inducing them to chemotaxis, secretion of proinflammatory cytokines tumor necrosis factor α (TNF), IL-1, IL-6, IL-8, the release of matrix metalloproteinases and other enzymes, the production of microbial antigens - specific immunoglobulins produced with the participation of chemokines involved T-and B-lymphocytes [15].

In addition to the induction of inflammatory changes in soft tissues proinflammatory cytokines activate osteoclasts, contributing to bone resorption of alveolar processes. Most of the known cytokines (such as IL-1, IL-2, IL-4, IL-5, IL-6, IL-8, TNF, IFN) are present not only in peripheral blood, but also in saliva. Sources of production of proinflammatory cytokines are built into the epithelium of the mucous membranes of lymphocytes and macrophages, as well as epithelial cells of the mucous membranes and salivary glands. It is known that the content of cytokines in saliva does not correlate with their level in the blood, which indirectly indicates their local synthesis.

2. Laser technologies in surgical dentistry. Effect of laser radiation on the pathogenesis of the wound process in the oral cavity

The use of dental lasers can be divided into the treatment of soft tissues, bone tissue and dental tissue. In the field of dental care a wide variety of lasers is used to improve the treatment of different diseases, a range of minimally invasive and practically painless procedures according modern standards of quality of dental care.

Various effects of laser radiation on dental tissues associated with the used wavelength and the irradiated substrate are clinically applied. This leads to many different modes of tissue removal, including photothermal and photoablation action. The heterogeneous structure of oral tissues changes optical properties depending on the cross-section plane, having a significant effect on the interaction with the laser beam. The benefits of laser coagulation-dissection compared to electrocoagulation are the less thermal tissue damage and the "smokiness" of the surgical field, as well as the biological effects of photo action on wound process [17].

The optimal combination of wavelength, mode and

the radiation power of lasers is determined in experimental studies [18]. Technical features of surgical lasers and modes of their use vary depending on clinical applications. Radiation power is adjustable radiation characteristics, which directly affects the achievement of clinical results. An important feature of laser thermal degradation is "controllability". Laser action is described by a number of equations, in particular, a biothermal equation that takes into account of the blood flow of the "heated" tissue, heat diffusion into adjacent soft tissues, radiation power, exposure, wavelength, absorption coefficient and other factors [19].

Lasers used in medicine are classified according to the type of active material, the method of energy consumption, wavelength and power of the generated radiation. The type of active material determines the wavelength of the generated radiation. Various chemical elements in different matrices allow us to distinguish more than 6000 varieties of lasers that generate radiation from the region of vacuum ultraviolet (0,157 μm) to the far infrared (>300 μm) range. The area of application of lasers with a wavelength from 0,5 to 2,0 μm in the fields of surgery is practically unlimited, there are a large number of literature sources that demonstrate the advantages of laser radiation in the treatment of various diseases. In surgery, depending on the characteristics of biological effects, lasers are divided into hemoglobin-absorbing (H-lasers) with a wavelength close to 1,0 μm and water-absorbing (W-lasers) with a wavelength close to 1,5 μm , operating in the infrared range of the light spectrum. There is a perception that the characteristics of the mechanisms of action of H - and W-lasers involve getting different results [20].

The effect of laser radiation on a biological object is considered as a multi-level process with specific mechanisms acting on different levels. A promising direction of dentistry is an objective characteristic of the wound process when using lasers, the study of the biological effects of surgical lasers, biochemical and immunological markers of regeneration and mediators of inflammation presented in the oral fluid and detected by laboratory methods, as well as the identification of concomitant signs of the disease, factors and determinants of the risk of the disease and its adverse outcomes [21].

According to the literature low-intensity laser irradiation accelerates the first phase of the wound healing process, stimulates the reaction of macrophages, cleansing wounds from purulent-necrotic masses, promotes early formation of granulation tissue and its fibrous transformation,

epithelialization of the wound defect and a reduction of treatment time, activates the biosynthetic function of fibroblasts, improves the processes of angio - and fibrillogenesis [15]. There is evidence of high efficiency of laser radiation in the rehabilitation of infected tissue, perhaps a combination of laser impact with the air-plasma flows under the nitrogen oxide therapy. Among the pathogenetic mechanisms of action of low-intensity laser radiation are considered: activation of cell metabolism and increase of its functional activity; stimulation of reparative processes; anti-inflammatory action; activation of blood microcirculation and increase of trophic tissue supply; analgesic effect; immune stimulating and immune modulating action; the reflex effect on the functional activity of organs and systems [22]. From the literature data the following changes in the biochemical composition of the oral fluid under the influence of a laser are known. A single laser exposure of 0,685 μm activates the synthesis of fibroblast growth factor β , insulin - like growth factor - 1 and BP-3 receptor. Effects of low intensity laser with a wavelength of 0,81-0,88 nm increases the content of IgA, IgG, IgM and lysozyme in the mixed saliva [23].

Microvessels are sensitive to photo effects. Biological effect of laser action on microvessels is photo dilatation and activation of the microcirculation in the tissues. The laser exposure activates the metabolism in microvessels surrounding the cells, increases the stability of the blood brain barrier, stimulates neoangiogenesis. The bio-stimulating effect of the helium-neon laser radiation is associated with the presence of a special photoregulatory system in the body, which has absorption bands in the red region of the spectrum. The impact of semiconductor lasers causes aseptic inflammatory reaction, stimulating the migration of cellular elements (fibroblasts, lymphocytes, monocytes), the appearance of fibrin clots. Fibroblast growth factors, vascular endothelial growth factor, collagen type IV, characteristic of the basal membrane of new vessels, α - and β -3- integrins are necessary for the adhesion of endothelial cells to extracellular matrix components. Neoangiogenesis and stimulation of the growth of the microvascular wall are shown [24].

It is assumed that the influence of a number of cytokines and growth factors leads to the mobilization and release of circulating progenitor cells of endothelium from the bone marrow, migrating to the sites of vascular damage and ischemia of tissues, partially included in the area of endothelial defect of the vascular wall and involved in angiogenesis. It is known that the stimulation of

angiogenesis by semiconductor lasers depends on the wavelength. The best results are obtained at a wavelength in the near infrared spectrum of 0,89 nm (GaAlAs laser). This wavelength is close to the peak penetration wavelength for biological tissues. The stimulating effect of infrared laser beams on regenerative processes has been demonstrated in trophic ulcers, infiltrates, wounds, bruises. Exposure to laser radiation optimizes local blood circulation and the fibrinolytic system of the blood. Laser radiation activating a number of enzyme systems increases the intensity of metabolic processes, promoting tissue regeneration. The action of low-intensity laser radiation activates the nuclear cytoplasmic structures, expressed, in particular, an increase in the surface of the nuclear membrane, the number of ribosomes and polysomes in the nuclear zone of the cytoplasm.

Diode lasers Er: YAG have demonstrated efficiency due to strong absorption of radiation by water. High power densities lead to evaporation of intra- and extracellular fluid. Because of this, diode lasers well cut, evaporate and coagulate the tissues while producing sterilization of the treated area. Nd: YAG laser is used in a similar way, however, has an excellent effect since the length of the laser's extension is 30 mm in water, which provides an advantage when stopping bleeding at a considerable distance from the irradiation area. In comparison with a scalpel for surgical incisions the diode laser doesn't crush tissue, decrease the severity of scarring and the time of epithelialization of the wound [25].

Removal of infected tissues using a diode laser at the stage of initial therapy should be carried out reasonably, taking into account the activity of the inflammatory process. The technical features of diode lasers are the removal of infected epithelium with *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum*, *Treponema denticola*, *Prevotella intermedia*, *Eikenella corrodens* integrated into it. At the same time, according to the literature data, there was no significant shift in the picture of the microbial landscape under laser irradiation of compromised tissue, however, a decrease in the frequency of detection of opportunistic strains and the absence of this effect on the nosocomial pathogens of *Pseudomonas* and *Proteus*, which connects with the lack of low-intensity laser irradiation of direct bactericidal action, stimulation of resistance of the body against low-aggressive strains of opportunistic flora [10].

RESUME:

It follows from the literature that an important component of clinical success in surgical dentistry is a favorable course of the wound process, the basis of which is regeneration. At the present level of development of surgical dentistry is not enough subjective characteristics in determining the clinical effectiveness of various methods. Objectively, the way of the wound healing process reflects the biochemical and immunological markers of regeneration and mediators of inflammation of the oral fluid. Data on a comprehensive study of the immunological reactivity of the body, the comparison of changes in its performance in various forms of inflammatory processes are virtually absented.

Currently, various devices in their technique and modes of laser radiation are used, while methodological information on the use of its in surgical dentistry is not enough. This has a negative impact on the frequency, effectiveness and safety of laser radiation, which causes reasonable uncertainty in practical dentists who do not have the appropriate conditions for the development of optimal techniques in practice. At the same time, the use of surgical lasers contributes to the economic and social effect. The urgency of the problem of comparative analysis of reparative processes depending on the method of surgical treatment and the need for further research expanding the practical use of modern, high-tech operations, with rapid rehabilitation of patients, reducing the number of complications, improving the results of treatment and cosmetic effect.

The reasonable choice of the instrument and its mode of operation for surgical intervention creates optimal conditions for the regeneration of tissues in the area of operation. In clinical practice surgical lasers are actively introduced, which, thanks to precise regulation of power and other parameters, create a minimum zone of thermal damage, which reduces the likelihood of complications (intra - and postoperative bleeding), the need for preoperative drug therapy, makes it possible to provide surgical dental care at a qualitatively new level.

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Abbreviation

Ig - immunoglobulin
IL – interleukin
µm – micrometer
nm - nanometer

TFR β 1 - transforming growth factor β 1

TLR- toll-like receptors

TNF - tumor necrosis factor

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