



## Characteristics of Changes in the Immunological Parameters of the Oral Fluid during the Treatment of Traumatic Injuries of the Mandible

Pulatova Shaxzoda Karimovna <sup>1</sup>

<sup>1</sup> Bukhara State Medical Institute Department of Surgical Dentistry

**Abstract:** Evaluation of the effectiveness of complex therapy of patients with mandibular fractures was carried out based on the results of an immunological study. Mandibular injuries have a negative effect on the activity of oral protection factors. As a result, we found it advisable to study the immunological parameters of oral fluid in patients and conduct a comparative analysis of them before starting treatment and after applying a set of therapeutic measures. Thanks to the data obtained from the immunological study, we were able to conclude that the proposed treatment regimen, which consists in fixing fragments of the lower jaw with cortical screws, applications of Traumel-C ointment and local exposure to infrared rays, is much more effective compared with traditional methods.

**Keywords:** mandibular injuries, reposition, fixation of bone fragments, fracture line, callus

**Relevance.** Currently, among all patients with maxillofacial profile, the number of victims with jaw fractures is 25-30%, of which 10-12% in combination with injuries to other organs and systems. The frequency of fractures of the mandible currently varies from 70 to 85% of the total number of injuries to the bones of the facial skull. At the same time, complications of injuries of this localization occur in about 15-25% of cases. The annual increase in the prevalence of mandibular fractures, as well as the aggravation of the nature of injuries, the increase in the number of multiple and combined injuries make the problem of improving the treatment of patients of the appropriate profile quite urgent [1.3.5.7.9.11.13].

Morphofunctional disorders that have developed as a result of trauma are largely aggravated by the presence of defects in the dentition (Lepilin A.V. et al., 2012). It is known that in patients after treatment of fractures of the mandible with a violation of the integrity of the dentition in 97.3% of cases, it is possible to detect signs of musculoskeletal dysfunction accompanied by limited movements in the temporomandibular joints, their asymmetry, pain during palpation of the masticatory muscles.

The rapid development of medicine, the improvement of methods for the diagnosis and treatment of diseases and deformities of the mandible requires modern research that meets the needs of practical dentistry at this level of its development.

**The purpose of the study** - study of the dynamics of immunological parameters of oral fluid under the influence of complex treatment of fractures of the mandibular bone.

**Materials and methods of research.** Clinical studies were carried out on the basis of the Department of Maxillofacial surgery of the Bukhara Regional Multidisciplinary Medical Center. The observations were based on a clinical and laboratory study of 157 patients diagnosed with mandibular fracture (single, double and multiple; unilateral and bilateral), of which 121 men (77.07%) and 36 women (22.93%) aged 18 to 75 years. The control group included 30 conditionally healthy individuals.

Primarily, taking into account the nature of the fracture of the mandible and the course of the post-traumatic period, all patients were prescribed complex treatment, the medicinal component of which consisted in therapy with broad-spectrum antibacterial drugs followed by selective administration of antibiotics, taking into account the composition and sensitivity of the microflora, detoxification therapy was prescribed to prevent complications of inflammatory etiology and accelerate the process of bone regeneration and included colloidal and crystalline solutions (5% glucose solution, salt solutions – 0.9% sodium chloride, hemodesis, rheopolyglucin, metrogil-100), desensitizing therapy was recommended to reduce allergic reactions that may accompany traumatic conditions, and included antihistamines such as diphenhydramine, suprastin, tavegil, diazoline, etc. In some cases, vitamin therapy was used to enhance general and local immunity. Symptomatic treatment included analgesics and nonsteroidal anti-inflammatory drugs to reduce pain, as well as other necessary remedies, depending on the clinic of the disease.

Based on the objectives of the study, depending on the type of local therapy, 157 patients with mandibular fractures were divided into 3 groups by random sampling:

The 1st (control) group consisted of 46 patients in whom local treatment consisted of bimaxillary splinting of the jaws with Tigerstedt splints and mouth rinses with a solution of the antiseptic furacilin in a dilution of 1:5000. For preventive purposes, antibacterial therapy was prescribed in the form of intramuscular injections of antibiotics of a number of cephalosporins - cefazolin, ceftriaxone, etc., having a bactericidal effect on gram-positive and gram-negative microorganisms. In cases of hematomas and pronounced edema of regional soft tissues, intravenous infusions of Metrogil (metronidazole, which has antibacterial and antiprotozoal effects) were used. In order to strengthen general therapy and prevent the development of dysbiosis, vitamin therapy was prescribed in the form of parenteral administration of vitamin preparations.

The 2nd group consisted of 54 victims, to whom applications of "Traumel-S" ointment were added to the above-mentioned local traditional medical complex;

The 3rd (main) group consisted of 57 patients who, after reposition and fixation of bone fragments of the mandible with cortical screws, included daily procedures of infrared radiation therapy (TII) and application of Traumel-C ointment containing active components of plant and mineral origin, in the form of application to apply it to the area of damage and massage until it is completely absorbed. The total number of patients is 157.

In this study, the effect of the drug Traumel-C on the regeneration process in mandibular fracture in combination with orthopedic treatment, antibacterial, detoxification and physiotherapy was studied. The drug was applied topically by applying and rubbing on the area of tissue integrity damage, and the procedure was performed once a day until completely absorbed, usually within 1-2 weeks, depending on the healing rate. After immobilization of bone fragments of the mandibular bone, the ointment was applied to a sterile gauze cloth and applied to the damaged area for local exposure. The study was also aimed at evaluating the effectiveness of the effect of Traumel-C on the process of tissue regeneration in fractures of the mandible [2.4.6.8.10.12.14].

In accordance with this scheme, local infrared therapy was used: local exposure to infrared radiation using a special device "INFRARED RADIATOR S.A. MED HOLDING OOO" manufactured in the Republic of Uzbekistan, with a wavelength of approximately 800 nm to 2500 nm and a main range in the region of 900-1000 nm, was used to improve the healing of fractures of the mandible. The radiation power varied from 20 to 200 MW/cm<sup>2</sup>, depending on the device model, and the duration of the procedure ranged from 10 to 20 minutes, depending on the patient's reaction.

The procedure was performed once a day, depending on the needs and individual characteristics of the patient, and the number of procedures depended on the severity of the fracture and the rate of tissue healing. Local therapy with infrared radiation made it possible to accelerate the processes of repair of regional tissues, reduce swelling and pain intensity of patients, as well as prevent the development of complications of a purulent – inflammatory nature by stimulating metabolic processes and cell regeneration in irradiated tissues.

The clinical effectiveness of local therapy of traumatic injuries of the mandible with infrared radiation was evaluated according to various criteria, including the timing of the formation of a callus (based on the indicators of radiation research methods), the degree of pain reduction, improvement of general condition, improvement of microcirculation, reduction of edema, acceleration of tissue regeneration, reduction of the risk of complications, as well as laboratory data. However, the effectiveness of therapy depends on various factors, including the type and characteristics of the fracture, the duration and treatment regimen, as well as the individual characteristics of the patient.

During the study of local immunity factors and enzymatic activity in the oral fluid, the following laboratory parameters were evaluated: the level of cytokines, including IL-1 $\alpha$ , IL-8, IL-1 $\beta$  and TNF- $\alpha$  (in mg/ml); IgA concentration (in mg/ml); phagocytic activity of neutrophils and others. To determine the cytokine level, oral fluid was taken before and after the orthopedic component of the complex treatment. The levels of interleukin-1 $\alpha$ , interleukin-1 $\beta$ , interleukin-8 and tumor necrosis factor- $\alpha$  were measured by solid-phase enzyme immunoassay using double antibodies and horseradish peroxidase. To compare the results, recombinant IL-1 $\alpha$ , IL-1 $\beta$ , IL-8 and TNF- $\alpha$  from a set of reagents from Bender medsystems, manufactured by Biochemack (Russia), were used. The results were recorded using a Multiscan\**mcc-340* photometer at a wavelength of 450 nm. The concentration of IL (in mg/ml) in the samples was calculated based on the calibration curve after measuring the optical density of the solution in the wells. The content of interleukin-6 was determined using the Interleukin-6-IFA-Best reagent kit (Vector-Best CJSC, Russia), and interleukin-8 was determined using the Interleukin-8-IFA-Best kit (Vector-Best CJSC, Russia).

To identify the features of the immunological status and objectification of the clinical picture, as well as to control the results of treatment, an immunological and biochemical study of the oral fluid and venous blood of patients was carried out, which consisted in assessing the cytokine profile, antibody levels, as well as determining the activity of enzymes.

Also, as part of the biochemical study, the activity of enzymes was determined, which reflect the functional state of organs and tissues, including bone tissue. For example, the level of alkaline phosphatase may reflect the activity of the processes of formation of new bone tissue. Biochemical methods are an important addition to other methods of monitoring the course of treatment of fractures of the mandible and allowed us to obtain more objective information about the condition of the patient's body and the effectiveness of treatment [15.17.19.21].

The activity of phospholipase A2 in oral fluid was determined using a modified Zubachik V.M. (2000) method and expressed in mmol/min/ml.

Cortical screws, metal (mainly titanium) fixing elements, were used to immobilize bone fragments in fractures of the mandible in the main group of patients. The procedure for using cortical screws was carried out in the operating room in sterile conditions with strict observance of the rules of asepsis and antiseptics. After the patient rinsed the oral cavity with an antiseptic solution (0.05% chlorhexidine solution), local conduction anesthesia of the upper and lower jaws was performed. When complete anesthesia was achieved, holes with a diameter of 0.2 cm were made in the area of the alveolar processes of the jaws using a physiodispenser with a tip and a boron at low speeds with water cooling. A screw with a length of at least 1.3 cm and a diameter of 2.4 mm was taken. Using a screwdriver, the screws were screwed into the intended point in each segment of the jaw, into the interdental spaces, between the roots of the central and lateral incisors, the first and second premolars, the first and second molars, while excluding contact of the screw with the roots of the teeth. To prevent injury to the mucous membrane of the upper and lower lips, the screws were

screwed in such a way that in the oral cavity the screw protruded above the mucous membrane by no more than 5 mm. Next, bone fragments were repositioned and jaws were compared in occlusion, wire or rubber rings were applied to screws to create an interjaw traction.

Rehabilitation included medication, a liquid diet, physical therapy and regular consultations with specialists.

The data obtained were processed using the generally accepted method of variation statistics. For this purpose, a software package specialized for biomedical research was applied. The data were entered into specially created tables in the Microsoft Office Excel 2010 program for the Windows XP operating system, as well as in the statistical software package Stat Soft Statistica v6.0. Data analysis was carried out using descriptive statistics. Statistical processing of the obtained data included the use of nonparametric methods, such as the Mann-Whitney criterion, and correlation analysis based on the Pearson criterion. The results were presented as a median, and the significance of the differences between the averages was assessed using the Student's criterion. The principles of evidence-based medicine were taken into account when conducting and organizing the study.

**Research results and their discussion.** In this study, the dynamics of the clinical course of the treatment process for fractures of the mandible was analyzed. A comprehensive assessment of the course of the treatment process for mandibular fractures was carried out on the basis of several factors and parameters: dynamics of clinical symptoms (assessment of changing clinical signs such as edema, pain, functional disorders and deformity); radiological data used to assess the degree of bone fragments reposition, callus formation (bone scar tissue) and fracture consolidation; laboratory indicators: (study of biochemical and immunological parameters); assessment of functionality, that is, restoration of important functions of the mandible.

The results of the study in different groups of patients are presented as follows:

After 2-3 sessions of infrared radiation therapy, patients in the main group showed a decrease in swelling, infiltration and hyperemia of soft tissues adjacent to the area of traumatic jaw injury, as well as a significant decrease in the intensity of pain during palpation. Against the background of the first procedure of infrared radiation therapy in the treatment of mandibular fractures, a number of positive effects were observed, including a decrease in edema by improving microcirculation and lymphatic drainage, a decrease in the intensity of pain in the fracture area and surrounding tissues, stimulation of cellular metabolism and collagen synthesis, improved blood supply and delivery of nutrients to damaged tissues, as well as a reduction in consolidation time fractures of the lower jaw. Due to the above-mentioned positive properties of infrared rays, a more or less complete regression of local signs of mandibular injury (except for determining the presence of a fracture line during X-ray examination) was determined at 4-5 sessions of physiotherapy, complementing complex treatment, and on 5-6 days after the start of therapy, signs of formation of connective tissue, that is, fibrous corns in the area of injury were noted during radiation examination the integrity of the mandibular bone (which is about a day ahead of the time of formation of such in patients of the control group). Repeated sessions of infrared laser radiation led to a further reduction in the time of formation of osteoid calluses in the area of localization of the fracture line. Improved microcirculation and lymphatic drainage, stimulated by infrared radiation, contributed to a more effective removal of excess fluid and a decrease in the volume of post-traumatic edema of soft tissues. The recommended treatment helped to reduce pain, swelling and restore the normal structure of bone fragments. Increased collagen synthesis and activation of cellular metabolism contributed to faster regeneration of damaged tissues and formation of bone structure [16.18.20.21].

A study on the effect of the combined use of Traumel-C ointment and infrared radiation procedures on the treatment of mandibular fractures has shown significant positive results. The use of Traumel-C ointment helped to reduce the severity of local signs of injury, stimulate tissue regeneration and improve microcirculation in the fracture area. This was accompanied by accelerated fracture healing, shorter rehabilitation time, and improved jaw functionality.

Higher treatment effectiveness was observed in the 3rd group of patients, who, along with traditional therapy, included applications of Traumel-C ointment and infrared radiation (AI) procedures in the

complex treatment. Additionally, infrared radiation procedures complemented the effect of Traumel-C ointment, contributing to a decrease in post-traumatic edema, improved blood supply, relief of pain and activation of cellular metabolism. On the 3-4 day of application of Traumel-C ointment, infrared radiation procedures and fixation of bone fragments by means of cortical screws in the treatment of fractures of the mandible, a decrease in edema in the fracture area was observed, manifested in a decrease in volume and an improvement in the appearance of adjacent tissues. In addition, this combination of therapy contributed to the activation of fracture healing processes, due to stimulation of tissue regeneration with Traumel-C ointment, improvement of blood supply and delivery of nutrients by infrared radiation, as well as ensuring stable fixation of bone fragments with cortical screws. This led to effective healing, reduced pain and increased stability of bone fragments in the fracture area, accelerating the regeneration process and improving the patient's quality of life. Patients also noted a decrease in the intensity of pain and discomfort, which was associated with a decrease in edema, better fracture healing and restoration of normal tissue structure. Thus, the combined use of Traumel-C ointment and infrared radiation procedures in combination with the use of cortical screws for 3-4 days of treatment of mandibular fractures demonstrates multiple beneficial effects, contributing to effective recovery and improvement of treatment results.

In the course of a study aimed at analyzing the dynamics of cytokines in the oral fluid in patients with mandibular fractures who underwent traditional therapy in conjunction with infrared radiation, the following results were obtained. After three days of treatment using infrared radiation, an average decrease in interleukin-1 $\alpha$  content was observed by 24.8%, which was  $18.2 \pm 1.3$  pg/ml compared with the baseline level of  $24.2 \pm 1.75$  pg/ml. A similar dynamics was observed in the concentration of other interleukins: the content of interleukin-1 $\beta$  decreased to  $15.9 \pm 2.31$  pg/ml, which is 49.7% less than the initial value of this indicator; and the content of interleukin-6 decreased to  $4.88 \pm 0.32$  pg/ml, which is 1.69 times lower than the initial level when patients were admitted to the department and so on.

The study revealed a different rate of decrease in cytokine content in oral fluid in patients with mandibular fractures who received traditional therapy and the drug Traumel-C. It was found that the level of interleukin-1 $\alpha$  on the third day of treatment decreased by an average of 2.16 times and amounted to  $11.2 \pm 0.87$  pg/ml, while before the start of treatment this indicator was  $24.2 \pm 1.75$  pg/ml. A similar dynamics was observed for other interleukins, for example, the level of interleukin-1 $\beta$  decreased to  $6.37 \pm 0.35$  pg/ml, which is a 4.96-fold decrease compared to the baseline value. Similar changes were noted for the level of interleukin-6, which decreased to  $4.22 \pm 0.15$  pg/ml, which is 1.97 times less than the value recorded at admission to the department, and so on.

Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), which is synthesized by monocytes and macrophages, is the primary mediator of inflammation. It initiates apoptosis (programmed cell death) and stimulates the production of interleukin-1 (IL-1), IL-6, IL-8 and interferon-gamma. TNF- $\alpha$  levels had similar dynamics to interleukins. The most noticeable decrease in TNF- $\alpha$  was observed in the third group of patients and amounted to  $12.5 \pm 0.2$  pg/ml, which is 8.8 times less than the initial values. In the first and second groups of the studied patients, TNF- $\alpha$  levels decreased by 4 and 1.72 times, respectively, which was less pronounced compared to the group of patients receiving complex treatment [14.15.16.17.18.19.20.21].

A decrease in the intensity of the destruction process in the oral mucosa, as well as a decrease in the number of cells with destructive changes in the oral fluid, contributed to a decrease in the activity of the enzyme phospholipase A2, which is involved in lipolysis (destruction of lipids).

Thus, the inclusion of Traumel-C ointment and AI sessions using cortical screws in the traditional treatment regimen for mandibular fractures makes it possible to restore immunological and biochemical parameters to normal values. This has a positive effect on clinical observations, as the length of stay of victims in the hospital is reduced, the process of formation of bone corns in the area of the jaw fracture line is optimized and the development of complications of infectious and inflammatory genesis is prevented.

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