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**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.3427964>Available online at: <http://www.iajps.com>**Research Article****IMPACT OF COMBINATION TREATMENT OF DRUG-ADDICTED PATIENTS WITH CHRONIC ODONTOGENOUS OSTEOMYELITIS OF THE JAWS ON MICROLymph FLOW OF GINGIVAL MUCOSA**¹Bezrukov S. G., ²Anosov M. S., ³Sayenko V. L., ⁴Zhad'ko S. I., ⁵Belousova A. M.¹Doctor of Medicine, Professor, Department of Surgical Dentistry and Maxillofacial Surgery - "V. I. Vernadsky Crimean Federal University" Medical Academy named after S. I.

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Aim. Number of drug addicted patients with chronic odontogenic osteomyelitis of the jaws is increasing year by year. The aim of this work was to study changes in on microlymph flow indicators in drug addicted patients in the course chronic odontogenic osteomyelitis treatment.

Materials and methods. Assessment of tissue blood flow in gingival mucosa in patients with chronic osteomyelitis was performed using Laser doppler flowmetry. All patients were divided into two groups: a treatment group and a control group. Sequestrectomy was performed to the patients from the treatment group with a bone defect closed with a concomitant use of PRP gel and FRP membranes. The same surgery was performed to patients from control group with closing a bone defect with iodoform tampon.

Results. During the study it was revealed that sequestrectomy with use of PRP gel and FRP membranes leads to rapid decrease in local postoperative inflammatory reactions, improvement of venous outflow and better functioning of microvessels endothelium, and, all in all, to optimization of the tissue healing process in drug addicted patients with chronic odontogenic osteomyelitis.

Keywords: odontogenous osteomyelitis of the jaws of drug-addicted, combination treatment, PRP-gel and FRP-membrane, flowmetry, lymph flow.

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INTRODUCTION:

Nowadays in Russia there is still high quantity of the patients with chronic odontogenous osteomyelitis associated with drug use. Long-term use of pervitin and desomorphine made from ephedrine- and codeine-containing mixtures is the main reason of the disease development [1, 2, 3].

These drugs are very toxic due to the high content of red phosphorus, iodine and other components required for release of pure substance [4].

The dose of ephedrine and codeine in self-made drugs is dozens of times higher than the therapeutic one. Therefore, long-term use of such narcotic substances causes persistent inhibition of the trophic function of the nervous system [5]. Red phosphorus compounds deposit in the calcified bone matrix causing the inhibition of osteoclast activity. Furthermore, dead osteocytes lose their ability to be replaced [6]. Moreover, hardening of the jawbone capillary network may lead to avascular necrosis [5]. Thus, long-term use of the above-mentioned drug-containing substances leads to osteomyelitis of the jaws with an atypical course [7, 8, 9].

The purpose of this research was to study changes in local microlymph flow indicators of drug-addicted patients with chronic odontogenous osteomyelitis by using different surgical approaches.

MATERIALS AND METHODS:

This work was done at Department of Maxillofacial Surgery in State Budgetary Healthcare Institution "Republic hospital named after N. A. Semashko" (Simferopol) from 2010 to 2018. During this study we did clinical and laboratory examinations of 44 patients (both males and females) aged from 24 to 52 years old (the average age was 36 years) diagnosed with chronic odontogenous osteomyelitis associated with use of pervitin and desomorphine. Patients were divided into two groups. The treatment group included 23 patients. We performed sequestrectomy operations with the closure of a bone defect with FRP-membranes and a PRP-gel for

the patients from the treatment group. This group included subgroup 1 (13 patients stopped taking narcotic drugs) and subgroup 2 (10 patients continued taking narcotic drugs). The control group included 21 patients. This group included subgroup 1 (12 patients stopped taking narcotic drugs) and subgroup 2 (9 patients continued taking narcotic drugs). We performed operations according to the conventional technique with the closure of the bone defect with iodoform tampon for the control group of patients.

During this study it was revealed that men had osteomyelitis (71%) more often, than women (29%). Patients used narcotic drugs at an average for 3,5 years. The disease duration varied from several months to 7 years. All patients used clandestine drugs with reference concentration of ingredients. Therefore, it was not possible for us to specify doses of ephedrine and codeine on 1 kg of body weight.

During the hospitalization to the Department of Maxillofacial Surgery patients were examined according to the standard scheme including clinical, radiological and laboratory methods (complete blood count, common urine analysis, blood sugar test, Wasserman reaction, AIDS testing and immunogram).

Patients' clinical examination included checkup of tissues and organs of maxillofacial area and neck, checkup of areas usually used for drugs injections - crooks of the arms, inner surface of the thighs, posterior triangle of neck, axillae and lower legs.

We performed recording of microlymph flow of gingival mucosa parameters with Laser doppler flowmetry (LDF) used double-channel laser analyzer of blood microcirculation computerized LAKK-OP (modification 2, "Lazma", Russia).

LDF is based on registration of changes in blood flow in microvasculature using non-invasive laser sensing of tissues with subsequent processing of the reflected radiation [11]. Infrared laser sensing with a wavelength of 0.78 μm was used to record the

parameters of blood flow. The probing gingival depth was 1mm.

Statistical processing of obtained data was performed using Wilcoxon signed-rank test and Mann–Whitney U test where $p < 0,05$ was considered statistically significant.

During the operative therapy we extracted causative teeth and non-viable bone tissue fragments that causes sensibilisation and chronic inflammatory process.

The local anesthesia was used for limited lesion of the jawbone and general (endotracheal) anesthesia was used for diffuse lesion of the jawbone. During the operative therapy we made trapezoid incision of the mucous membrane. Then we skeletonized the area of the affected bone to visually unchanged tissues removing sequestra, broken teeth and non-viable bone tissue fragments. We filled the bone defect with iodoform tampon after using antiseptics to treat surgical wounds for the patients from the control group. The end of the tampon was brought into the oral cavity [10]. All patients from the treatment group were injected with PRP-gel using an injection needle (G18). Injections were given subperiosteally and intraosseously under pressure into the spongy substance of the wound edges along the periphery of the bone defect. The bone defect was filled with FRP membranes. Then, as the circumstance arises, we advanced and mobilized mucoperiosteal flap with the closure of the bone defect and suturing of the wound with biodegradable suture material (Vicryl 3-0) layer-by-layer [11].

We made wounds dressing daily and removed the stitches after 9 days. The iodoform tampons were periodically tightened and changed for the control group patients until the bone defects were fully epithelialized. We provided recommendations on proper oral hygiene measures to all patients. Conservative treatable included antibacterial and anti-inflammatory therapy, prescription of immunostimulatory drugs and multivitamins.

RESULTS AND DISCUSSION:

Values recorded in healthy individuals in similar areas of the gingival mucosa were considered as statutory values of tissue lymphodynamics.

Average values of indicators of tissue lymphodynamics (both in treatment and control groups) recorded before the surgical treatment were close, comparable and did not differ significantly, therefore we found it possible to use these data as baseline for both comparison groups.

During the preoperative stage the amplitude maximum was recorded in the range of respiratory

rhythms. That indicates an increase in venous blood filling up to the prevalence of stagnant processes in postcapillary and capacitance microcirculatory vessels. Sharp increase of the perfusion level along with high amplitude value of the respiratory undulation on the background of depression of other rhythms indicated significant venous hyperemia associated with hypertonus of the inflow vessels accompanying the chronic inflammatory process. Clinically, this was expressed in local hyperemia and edema. Thus hypertonus of the inflow vessels on the background of endothelial dysfunction accompanied by venous hyperemia and tissue edema was revealed in the patients with chronic odontogenous osteomyelitis at the preoperative stage.

Re-registration of tissue hemo - and lymphodynamics indicators was carried out at the end of 1st, 6th and 12th months after surgery.

During postoperative supervision intergroup differences in tissue hemo-and lymphoperfusion indicators were detected, in comparison both with the preoperative period indicators and reference values. It is found that dynamics of hemo - and lymphodynamics indicators in patients at early preoperative stage depended on the approach of surgical treatment. At the late preoperative stage these dynamics depended on the length of drug use or withdrawal from drugs while approaching in some cases to standard values (Figure 1).

We assume that total increase in endothelial activity was recorded due to the stimulation of angiogenesis and the emergence of new collateral vessels in the treatment group in the early postoperative period. This was evidenced by a significant increase in the amplitude values of endothelial rhythms. These positive changes were not observed in the absence of platelet-derived growth factor in the early postoperative period in the control group.

The obtained data indicated that use of PRP-FRP-technologies significantly reduced the severity of inflammatory reactions in the lesion and tissue edema and promoted initiation of reparative regeneration at an early stage of the postoperative period.

Moreover, absence of statistically significant intergroup differences in tissue lymphodynamics and hemodynamics showed that use of PRP-FRP-technologies caused similar positive changes in patients stopped taking drugs and continued to use drugs (Fig. 1A).

Comparative assessment of spectral characteristics of tissue blood flow shows significant difference in amplitude values of myogenic rhythms among

patients stopped taking drugs and continued to use them.

The average amplitude values of myogenic rhythms in patients stopped taking drugs were comparable to the standard values (10,22 perf. un. with p_1 and $p_2 > 0,05$) both in the treatment (10,95 perf. un.) and

control (10,48 perf. un.) groups. These values were by a third ($p < 0.05$) higher than the similar indicators registered among groups of patients continued taking drugs (Fig. 1B). It should be noted that the increase in amplitude values of myogenic rhythms showed a significant decrease in peripheral resistance in smooth muscle precapillaries.

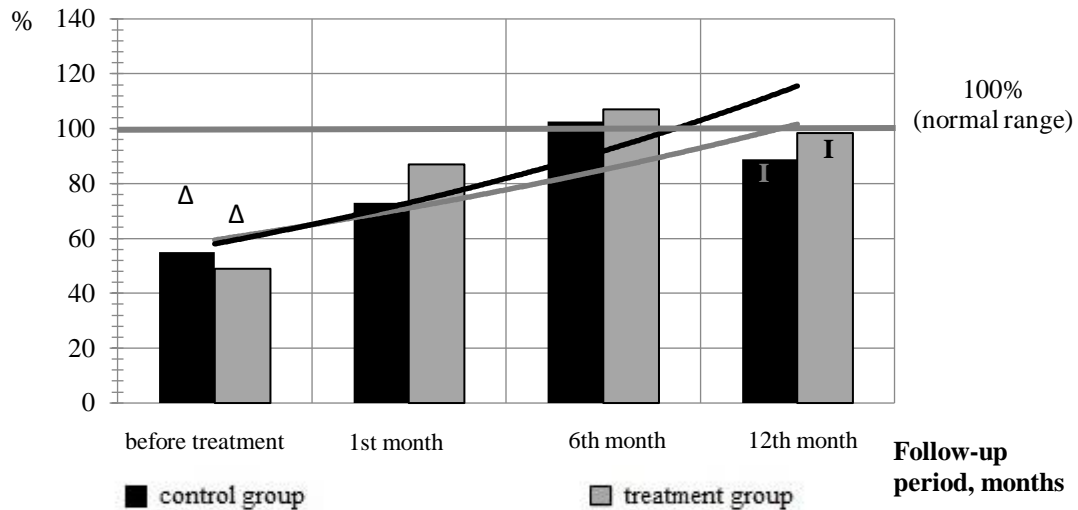


Figure 1A. Diagram and graphic representation of dynamics of amplitude values of myogenic rhythms in patients both from treatment and control groups before treatment and during the entire observation period expressed as a percentage: patients stopped taking drugs.

Notes: Δ- statistical processing of the obtained data has been conducted with Mann-Whitney U test, where p-value $p < 0,05$ was considered statistically significant.

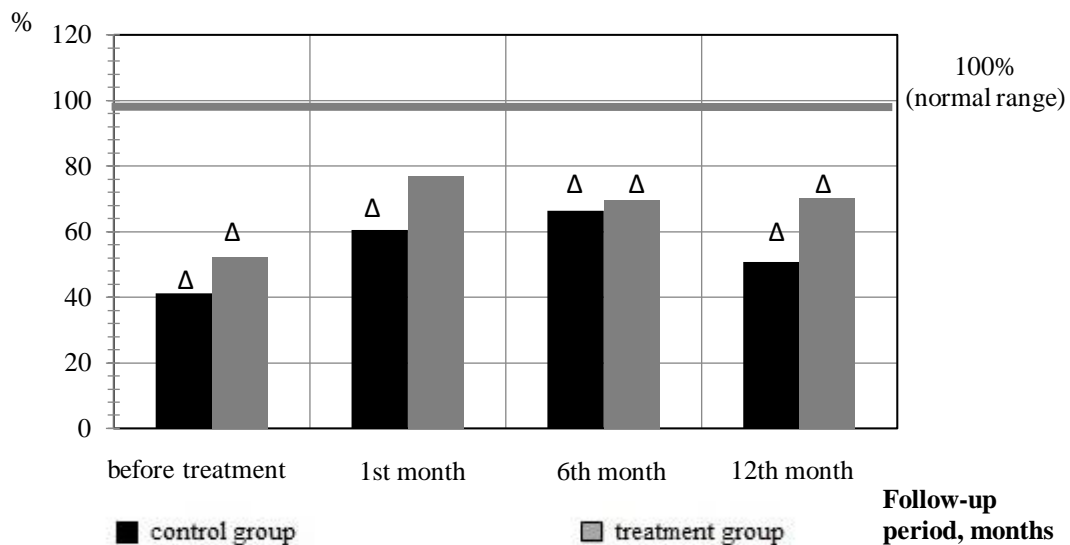


Figure 1B. Diagram and graphic representation of dynamics of amplitude values of myogenic rhythms in patients both from treatment and control groups before treatment and during the entire observation period expressed as a percentage: patients continued taking drugs.

Notes: Δ- statistical processing of the obtained data has been conducted with Mann-Whitney U test, where p-value $p < 0,05$ was considered statistically significant.

Spectral characteristics of the lymph flow had resonant behavior in the pacemakers area of phase oscillations (avg. – 17,64 rel. un.) and were close to the standard values (15,64 rel. un.). Hyperemia (including venous) and excessive tissue edema were not observed in the patients stopped taking drugs. At the same time, activation of nutritional blood flow was registered due to optimization of the reparative regeneration process without signs of local inflammation.

CONCLUSION:

1. Progression of chronic osteomyelitis in drug-addicted patients was accompanied by impaired lymph flow. It is evidenced by higher levels of micro lymphoperfusion (0,27 rel. un.) compared with the corresponding data recorded in healthy patients (0,13 rel. un.).

2. Surgical treatment (sequestrectomy) with use of PRP and FRP technologies in drug addicted patients with chronic odontogenic osteomyelitis leads to a rapid decrease of local postoperative inflammatory reactions, improvement of the lymph flow, and, all in all, optimization of the healing processes and tissue regeneration.

3. The nature of functional changes in the lymphatic bed in the examined patients corresponds to the inflammatory and dystrophic reactions of osteomyelitis of the jaws. Disease indicators tend to increase compared with the norm and initial values with the progression of the disease. The analyzed parameters of tissue blood flow had significant upward trend, more in the treatment group, during the treatment course and withdrawal from drugs.

List of symbols and Abbreviations

PRP – platelet rich plasma

FRP membrane – fiberglass pressure vessel membrane

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