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# INSOMNIA IN PANIC DISORDER. LITERATURE REVIEW

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## SUMMARY

Sleep disorders and panic disorder (PD) are often comorbid and closely interrelated. Sleep disorders aggravate the severity of panic disorder, and pathological anxiety worsens sleep. In this regard, the treatment of insomnia in patients with PD is aimed at harmonizing the emotional state and correcting sleep and, along with pharmacotherapy, includes a wide range of psychotherapeutic methods. Successful treatment of insomnia increases the effectiveness of PD therapy, reduces the likelihood of relapse and increases the susceptibility of patients to many anti-anxiety drugs.

**KEYWORDS:** sleep; insomnia; panic disorder; panic attacks

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## ИНСОМНИЯ ПРИ ПАНИЧЕСКОМ РАССТРОЙСТВЕ

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## РЕЗЮМЕ

Нарушения сна и паническое расстройство (ПР) часто коморбидны и тесно взаимосвязаны. Нарушения сна усугубляют тяжесть панического расстройства, а патологическая тревога ухудшает сон. В связи с этим лечение инсомнии у больных с ПР направлено на гармонизацию эмоционального состояния и коррекцию сна и, наряду с фармакотерапией, включает широкий спектр психотерапевтических методов. Успешное лечение инсомнии повышает эффективность терапии ПР, снижает вероятность рецидива и повышает восприимчивость больных ко многим противотревожным препаратам.

**КЛЮЧЕВЫЕ СЛОВА:** сон; инсомния; паническое расстройство; панические атаки.

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## Introduction

Panic disorder (PD) is a widespread problem in modern society, especially in metropolitan areas. According to different authors, the prevalence of PD in the population is 2–5 %, and it most often develops in young people (the average age is about 25 years) [1].

The modern view on the etiology and pathogenesis of PD suggests the involvement of various factors in it: predisposing (genetic and constitutional), accelerating (provoking) and fixing (Table 1) [1].

### *Clinical manifestations of panic disorder*

In ICD-10, PD is coded with the index F41.0 (episodic paroxysmal anxiety) and is included in the class «Neurotic,

stress-related and somatoform disorders» (F40-F48) [2]. It manifests as unexplained, distressing attacks of intense fear and/or feelings of internal tension combined with various autonomic (somatic) symptoms that peak within a few minutes. Currently, the DSM-IV and ICD-10 have adopted the following criteria for establishing the diagnosis of PD [2, 3]:

A. Recurrent attacks in which intense fear or discomfort combined with 4 or more of the following symptoms develops suddenly and peaks within 10 min:

- throbbing, palpitations, rapid pulse;
- sweating;
- chills, tremors;
- shortness of breath, dyspnea;

Table 1  
**Insomnia development factors**

| Factor type  | Factors                                                               | Mechanisms                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------|-----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Predisposing | 1) Genetics<br>2) Pathophysiology<br>3) Personality<br>4) Environment | <ul style="list-style-type: none"> <li>abnormal norepinephrin and GABA metabolism;</li> <li>abnormal neurodynamics;</li> <li>medical conditions</li> <li>early life state</li> <li>city living</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                     |
| Provoking    | 1) Mentality<br><br>2) Biology<br><br>3) Physical health              | <ul style="list-style-type: none"> <li>conflict peak (a divorce, painful discussions, or leaving one's family);</li> <li>acute and potent stressors (a loved one's death, an illness, or an accident);</li> <li>abstract identification or contraposition (movies, books, etc.);</li> <li>hormonal changes (pregnancy, delivery, weaning, or climacteric);</li> <li>sexual debut, intake of oral contraceptives, or abortion;</li> <li>menstrual cycle (its disorders or the final phase);</li> <li>alcohol abuse;</li> <li>weather effects;</li> <li>excessive physical exercise;</li> </ul> |
| Fixing       | 1) Behavioral<br>3) Cognitive distortions                             | <ul style="list-style-type: none"> <li>avoidance behavior;</li> <li>perception and thinking distortion that prevents one from normal perception of reality.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                        |

Table 2  
**PDs classification**

| Criterion                                              | Variants                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Based on panic-associated symptoms                  | <ul style="list-style-type: none"> <li>major/massive panic attacks (4 or more symptoms; daily or monthly); minor panic attacks (less than 4 symptoms; several times a day);</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                            |
| 2. Based on the main attack component                  | <ul style="list-style-type: none"> <li>vegetative (mostly vegetative disorders with undifferentiated phobias);</li> <li>hyperventilation (frequent and deep breathing, reflex apnea, paresthesias, and muscle pain associated with respiratory alkalosis);</li> <li>phobic (mostly phobias associated with fears in the situations the patient considers as triggers);</li> <li>conversion (hysterical conversion disorders, often senesthopathies, no or mild fear and anxiety);</li> <li>senesthopathic (mostly senesthopathies);</li> <li>affective (pronounced depressive or dysphoric disorders);</li> </ul> |
| 3. Typicality-based                                    | <ul style="list-style-type: none"> <li>typical panic attacks (all vegetative and affective main symptoms);</li> <li>atypical panic attacks (no or atypical affective manifestations and some additional symptoms, particularly globus pharyngeus, limb weakness, abnormal vision, hearing, gait, speech, and/or voice, syncope, body bending, cramps, nausea, vomit, and/or abdominal discomfort);</li> </ul>                                                                                                                                                                                                     |
| 4. Based on presence/absence of associated agoraphobia | <ul style="list-style-type: none"> <li>with agoraphobia;</li> <li>without agoraphobia.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

- respiratory difficulty, a choking sensation;
- pain or discomfort in the left side of the chest;
- nausea or abdominal discomfort;
- dizziness, instability when walking;
- weakness, lightheadedness, fainting spells;
- numbness or tingling sensation (paraesthesia);
- hot and cold flashes;
- feelings of derealization, depersonalization;
- a fear of dying;
- a fear of losing one's mind or acting uncontrollably.

B. The occurrence of panic attacks (PA) is not due to the direct physiological effects of any substance (e.g., drug dependence or medication intake) or somatic disease (e.g., thyrotoxicosis).

C. In most cases, PAs do not arise from other anxiety disorders such as phobias (social and simple), obsessive-phobic disorders, post-traumatic stress disorder.

Different variants of the classification of PDs depending on the parameters taken as a basis [1, 4] are given in Table 2.

The main manifestation of PD is PA or vegetative crisis, which are not confined to a particular situation or circumstance and are therefore unpredictable. The attacks (sudden episodes of severe anxiety) usually last from 1 min to 1 hour and occur on average 2–4 times a week.

Panic paroxysms in themselves are not dangerous to life or health, but they frighten the patient to such an extent that he or she loses control over feelings and emotions and becomes completely defenseless. PD patients gradually lose self-confidence and faith in others, the strongest feeling of insecurity does not allow them to communicate normally with other people. A PD patient avoids places where it is difficult to get help, and in congested and crowded places, as well as in confined spaces, he or she prefers to be accompanied by friends or family members (agoraphobia) [5].

Long-term restrictive (selective) behaviour leads to severe social disability or social demoralisation, followed by the development of secondary depression. The fixation on somatic symptoms arising in PA forms in patients' specific fears (of heart attack, stroke, fainting, etc.), often taking on a compulsive character and eventually leading to the development of obsessive-phobic or hypochondriac syndrome.

#### *Comorbidity of panic disorder and insomnia*

The study of the representation of insomnia in patients with PD shows, first, a high frequency of their comorbidity [6–8]. According to different authors [9–11], insomnia occurs in 60–80% of patients with PD. At the same time, both pathological conditions have a more complex interaction rather than a unilateral one.

Firstly, they share common emotional, personal, and biological backgrounds. For example, many people suffering from insomnia have high levels of neuroticism, introversion, anxiety, and perfectionism, which is also characteristic of patients with PD [12–15]. Biological studies have shown the role of polymorphism of certain genes of the serotonergic system in the pathogenesis of both PD and insomnia [16, 17]. Social and psychological stressors, which are considered the

leading provocateur of insomnia development, also lead to the occurrence or increase in the frequency of PA [18, 19].

Second, PD and insomnia share similar factors and mechanisms of pathogenesis. The modern neurocognitive model of insomnia, like PD, is based on Spielman's 3Ps model (pre-disposing, precipitating, and perpetuating) [20].

Thirdly, being comorbid conditions, PD and insomnia aggravate and make each other chronic. A clear dependence of disease severity on concomitant sleep disorders has been shown [21, 22]; at the same time, sleep disorders are caused by pathological anxiety, which is manifested by cortical hyperactivation, which, in turn, is the main link in the pathogenesis of insomnia [23].

Specialists underestimate the problem of insomnia. This is because patients with PD rarely report their sleep disorders to a physician, listing more vivid, dramatic, and frightening PAs in the list of complaints, as well as the fact that physicians rarely actively question patients about their sleep disorders [24–26].

#### *Features of insomnia manifestation in panic disorder*

Patients with PD complain of difficulty falling asleep, disturbing thoughts before going to bed, and non-restorative sleep [9].

Only 25 % of patients have PAs exclusively during waking hours. The majority of PAs, single or repeated (30–45 %), occur during nighttime sleep. More than half (54 %) of patients report attacks during both waking and sleeping periods, and in 21 % of patients PAs occur only during sleep [9, 10]. PAs arising from sleep exhibit all the symptoms characteristic of PA [27] and at the same time have certain specific features: they are shorter in duration, have more pronounced phobic and psychosensory manifestations, and less pronounced vegetative symptoms in the seizure structure [10]. Fearing the recurrence of PA, patients deliberately deprive themselves of sleep, which aggravates insomnia and generally blight these patients' life. Consequently, nocturnal PAs lead to more pronounced social maladaptation and are considered as an indicator of a more severe course of the disease [9, 10, 27].

M. Van de Laar et al. published data on the fact that in the joint manifestation of PD and insomnia aggravate the disease, reduce the effectiveness of therapy, and increase the probability of recurrence of PD and the risk of suicidal behaviour [13].

Polysomnographic study of patients with PD, according to

Table 3  
**Sleep of PD patients and healthy subjects [29] (M ± SD)**

| Parameter                                 | PD patients (n = 24) | Healthy subjects (n = 24) | p       |
|-------------------------------------------|----------------------|---------------------------|---------|
| Sleep latent period (before phase 2), min | 20.0 ± 10            | 10.9 ± 5                  | < 0.001 |
| Sleep effectiveness, min                  | 90.9 ± 4             | 94.2 ± 6                  | < 0.01  |

Table 4  
**Gross movements in PD patients and healthy subjects during sleep (seconds per sleep hour) [29] (M ± SD)**

| Sleep phase | PanD patients (n = 24) | Healthy subjects (n = 24) | p      |
|-------------|------------------------|---------------------------|--------|
| Phase 1     | 30.3 ± 32              | 10.9 ± 25                 | < 0.02 |
| Phase 2     | 38.3 ± 37              | 13.2 ± 21                 | < 0.01 |
| REM sleep   | 16.4 ± 19              | 5.8 ± 11                  | < 0.05 |

most studies, reveals increased bedtime, frequent awakenings, decreased sleep efficiency and reduced total sleep duration [23, 28–30]. T. Uhde et al. examined 9 patients with PD who did not take medication for 2 weeks [31]. The authors showed that patients had increased motor activity during sleep, decreased latent period of the sleep phase with rapid eye movements (REM) and decreased REM density (REM frequency per unit time) compared to the corresponding parameters of healthy control subjects. L. Pecknold et al. found poor sleep efficiency in 84 ± 12 % of patients with PD (n = 44) [28]. A survey of patients with PD conducted by P.J. Hauri et al. showed lower sleep efficiency and increased motor activity, in particular, due to the number of large movements, compared to the control group (Tables 3, 4) [29].

Only a few studies have polygraphically recorded PAs arising from sleep, and these data, as well as the authors' conclusions about the mechanisms of sleep, are contradictory. I. Lesser et al. recorded PA arising directly from delta sleep, which allowed them to suggest a commonality between the mechanisms of PA during sleep and nocturnal fears [32]. E. Mellman et al. recorded 6 PAs during sleep, all of them arising from the 2nd or 3rd stages of sleep [33]. S. Bell et al. found an increased frequency of nocturnal PAs in patients who also suffered from isolated sleep paralysis, which led the authors to think about a possible connection between nocturnal PAs and REM sleep phases [34].

In the study by R. Hauri et al. [8] PA attacks occurring in sleep were recorded, 6 of them in the transitional phase between stage 2 and stage 3 sleep [29]. According to the authors' observations, these attacks are unique, different from nocturnal fears and from the anxiety state in sleep. Thus, the patient's awakening and the panic paroxysm itself were preceded in most cases by eye movements during slow-wave sleep, muscle twitching, increased muscle tone, and increased EEG frequency up to 21 Hz. According to the authors, nocturnal PAs are more similar to nightmares of patients with posttraumatic stress disorder.

There is an opinion that disorders of the current functional state of the brain in the sleep-wake cycle play a key role in the initiation of PA. The imbalance of inhibitory and activating non-specific brain systems (excessive activity of the waking system, insufficiency of synchronising mechanisms) is considered as the main pathogenetic factor, which is combined with anxiety-phobic disorders and suprasegmental autonomic activation with hypo-function of predominantly parasympathetic innervation in the cardiovascular system. If we proceed from this point of view, the excessive activity of the waking system can be manifested either during the waking period or during the transition period from daytime wakefulness to sleep during the first and second sleep cycles. This sets the stage for the occurrence of either wakefulness PA, sleep PA, or a combination of the two. This has been confirmed by polygraphic analysis of the cyclic organisation of nocturnal sleep with assessment of the duration and percentage representation of sleep stages, as well as the correlation between electrophysiological parameters and sleep stages [10, 23].

The degree of sleep structure disturbance in PD is different [10]. When PA occurs only in wakefulness, sleep is not grossly altered. In this case, as a rule, there is an increase in nonspecific activation of electroencephalogram (EEG) during wakefulness and sleep. More pronounced sleep disturbances are noted when PA is present during sleep and wakefulness or only during sleep. PAs usually occur in stage 2 sleep and delta sleep. In sleep PA,

there are signs of increased autonomic and EEG activation in relaxed wakefulness, before falling asleep and during spontaneous nocturnal awakenings, and there are characteristic disturbances in the structure of sleep, affecting the REM and delta sleep phases. In the presence of sleep PA and wakefulness PA, maximum disturbances in the sleep structure affecting all stages of sleep (rapid, light and deep slow-wave) were noted.

Hyperventilatory manifestations occurring during sleep PA (awakening from a sensation of inability to inhale or exhale, forcing the patient to jump out of bed, open the window; dizziness and clenching of the fingers, etc.) often give specialists reason to suspect the presence of obstructive sleep apnea syndrome. Diagnostic guidelines in this case are the persistence of the sensation of shortness of breath for more than a few seconds after awakening, the vivid emotional colouring of the attack, and the data on the presence of similar attacks during the day, which makes the diagnosis of «true» sleep apnea unlikely. The final answer is given by nocturnal polysomnography with recording of respiratory parameters during sleep [23].

#### *Approaches to the treatment of panic disorder*

Clinical evidence suggests that therapy for PD should take into account its diurnal distribution and the presence and nature of associated sleep disorders.

Traditionally, the treatment of PD consists of several steps:

1. PA management;
2. basic therapy for PD, aimed at preventing recurrence of PA and correcting emotional state;
3. relapse prevention.

Benzodiazepine tranquilisers have the most rapid effect in the treatment of PA, allowing the seizure to be terminated in 15–20 minutes. However, with prolonged use, the dose of the drug has to be increased over time, and irregular use and the associated rebound phenomenon may increase the frequency of seizures over time. Therefore, this group of drugs is not suitable for basic long-term therapy of PD aimed at preventing seizure recurrence and reducing anxiety. Clinical observations show that antidepressants (selective serotonin or serotonin–norepinephrine reuptake inhibitors), which are characterised by high efficacy, good tolerability, ease of prescription, low toxicity in overdose and absence of addiction and dependence effects in long-term use, are the closest to the level of an ideal antipanic drug. Drugs of this group control not only PA, but also other psychopathological syndromes formed in patients with PD [35]. Taking into account these features, the above drugs are recommended as the drugs of choice in PD with or without agoraphobia [36, 37].

In patients with therapy-resistant PD, the 2nd generation antipsychotics olanzapine [38] and risperidone [39] have been shown to be effective. Beta-adrenergic blockers (propranolol and atenolol) are particularly effective in the severe vegetative component of PD, as they block the physical symptoms of chest pain, tightness in the throat and dyspnoea without sedation.

Psychotherapy is an integral component of PD therapy, which is used both independently and in combination with pharmacotherapy. The effect is often achieved only with the help of psychotherapy [40, 41].

Therapeutic tactics are determined by various factors, particularly the severity of the condition. Mild PD (relatively infre-

quent PAs not accompanied by persistent avoidant behaviour) allows psychotherapy in isolation or in combination with small, fixed doses of daily anxiolytics administered in short courses (no more than 3–4 weeks). Severe PD (more than 4 PAs per month, obvious expectancy anxiety, agoraphobia impairing social adaptation; mild or moderate comorbid depressive disorder) suggests monotherapy for 3–6 months. It is also possible to add a benzodiazepine drug for the initial 2–4 weeks of treatment as an effective «bridge» until the desired effect of selective serotonin reuptake inhibitors is realised [21, 42].

#### *Treatment of sleep disorders in patients with PD*

International recommendations for the treatment of insomnia suggest the use of psychotherapy as the leading method of treatment of chronic insomnia, as well as pharmacological agents – not only hypnotics, but also a wide range of anti-anxiety drugs (antidepressants and neuroleptics) that have a positive effect on sleep [43]. Thus, all of the above-mentioned methods of treating PD to a greater or lesser extent influence human sleep by facilitating falling asleep, reducing the number and duration of nocturnal awakenings, and thereby acting on the recovery processes occurring during night sleep.

Psychotherapy is the leading method of therapy for chronic insomnia, which improves sleep no less effectively than medications [44, 45]. At the same time, the effect of medications on sleep often ceases almost immediately after the end of the medication, while the results of normalising sleep patterns with the help of psychotherapy are maintained in the future. In addition, psychotherapy does not cause addiction or side effects, which is often observed with the use of sleeping pills.

Among the psychotherapy methods effective in treating both PD and insomnia, cognitive-behavioural psychotherapy should be highlighted. According to most international guidelines for the treatment of insomnia, cognitive-behavioural therapy for insomnia is the method of choice in the treatment of this category of patients [1, 46]. According to a number of studies, cognitive-behavioural therapy for insomnia comorbid with PD leads to decreased PA and improved sleep [1, 6].

Other non-pharmacological methods effective in the treatment of insomnia include: exposure to bright light during the day; water procedures, especially baths with substances that have a calming effect (pine needles, sea salt, special bath foam, etc.); aromatherapy in the form of massage with essential oils, inhalations, vapours and aromatic baths, sleeping herbal pillows; massage and acupuncture; therapeutic music and «nature sounds». An important and necessary condition for the effectiveness of any therapeutic intervention for insomnia is sleep hygiene [45].

It is important to remember that insomnia itself can increase anxiety and worsen well-being and mood, usually in the morning hours after poor sleep [47]. At the same time, PA in sleep disrupts falling asleep to the point of recurrent sleepless nights. Therefore, short courses of sleeping pills may be justified when the clinical picture is dominated by symptoms of insomnia. Drugs affecting the hamergic system are more often used, as they facilitate falling asleep, reduce the waking time within sleep, and improve recovery processes during sleep.

The most modern hypnotics are derivatives of cyclopyrrolones (zopiclone), imidazopyridine (zolpidem) and pyrazolopyrimidine (zaleplon). These drugs have, in addition to hypnotic, sedative, anxiolytic, anticonvulsant and myorelaxant action, have a short half-life, with proper use do not cause addiction and daytime wakefulness disorders, unlike benzodiazepines. Nevertheless, given the rapid onset of effect and anti-anxiety effect, in the treatment of this category of patients derivatives of benzodiazepines in some cases it is advisable to use a short course (no more than 2–3 weeks). It should be borne in mind that prolonged use of any sleeping pills, even of the modern generation, can cause addiction and form dependence, as well as contributes to the development of insomnia itself. Therefore, it is not recommended to take sleeping pills for more than 3 weeks.

Alternatives to hypnotics in the modern drug market are non-drowsy drugs of other pharmacological groups positively affecting sleep: anxiolytics, antidepressants and antipsychotics, antihistamines. Low-dose antidepressants and some neuroleptics [48, 49] can improve sleep in patients with anxiety disorders and insomnia without clinically significant depression. Among antidepressants, tricyclic (tetracyclic) nonselective antidepressants (imipramine, clomipramine, amitriptyline, mianserin, maprotiline) and selective antidepressants (selective serotonin reuptake inhibitors – paroxetine, fluvoxamine, sertraline, fluoxetine, citalopram) are used in the treatment of insomnia; among neuroleptics, levomepromazine, chlorpromazine and quetiapine are more commonly used. These drugs do not develop addiction and physical dependence.

Doxylamine succinate (DS), which acts simultaneously on M-cholinergic and H1- histamine receptors in the central nervous system, is often used among drugs with a sedative effect. Such a combined effect on receptors contributes to the enhancement of the sleeping effect and the development of sedative action of DS. Treatment of insomnia with DS is effective and safe, which is shown in many foreign and domestic studies [50, 51, 52]; it is the only sleeping drug that can be used during pregnancy. An examination of 61 patients with various forms of neurotic disorders, including PD with sleep disorders, conducted in the clinic of the Department for the Study of Borderline Psychiatric Pathology and Psychosomatic Disorders of the The Mental Health Research Centre (MHRC) of the Scientific Organizations Federal Agency, showed the efficacy and safety of DS in the treatment of this category of patients [52].

A convenient form of DS is offered by the German company «Krevel Miselbach»: Valocordin-doxylamine – drops for ingestion. 1 ml of the drug contains 25 mg of DS. The drug has a mint smell, giving an additional sedative effect. The advantage of the liquid form is that the drug can be dosed more flexibly than DS in tablets. The possibility to choose an individualised dose contributes to increased compliance. The fractional patented dropper simplifies dosing. The recommended single dose for patients over 18 years of age is 22 drops (corresponds to 25 mg DS). In case of insufficient efficacy of therapy, the dose can be increased to a maximum of 44 drops (50 mg DS).

In recent years, scientists have shown great interest in the study of the sleeping properties of melatonin. Synthetic analogues of melatonin allow normalising the level of this

hormone in the central nervous system. They are quite effective and harmless sleeping pills, which can be recommended in all cases of sleep disorders, in patients of any age and with any concomitant pathology without visible negative effects and with a high degree of tolerability [44].

Among other drugs with a sleeping effect for the treatment of insomnias, remedies based on individual herbs or herbal compilations, which are the basis of combined phytopreparations, are prescribed.

The treatment regimen is determined individually depending on the nature and severity of the symptoms of PD and insomnia. The use of drug-free methods should be considered a priority in treatment. Drug therapy should be used if non- pharmacological correction is ineffective. In milder variants of PD, treatment of insomnia should preferably begin with psychotherapy in combination with herbal sleeping pills and melatonin preparations. They are the group of choice for young people, cause the least problems for the patients taking them and can be easily discontinued later. If these drugs are ineffective within 3–5 nights, they are replaced by more potent – modern sleeping pills with minimal risk of drug dependence and addiction (doxylamine, zopiclone, zolpidem, zaleplon). Use immediately medication treatment should be used in patients when the rapid onset of effect is important. For more severe symptoms, a combination of psychotherapy and psychopharmacotherapy is recommended, including drugs from the groups of antidepressants and neuroleptics, whose therapeutic targets are both PD and sleep disorders, and which are acceptable for long-term use without the risk of addiction and dependence.

Successful treatment of insomnia has been shown to increase the efficacy of PD therapy, reduce the likelihood of relapse, and increase patients' susceptibility to many anti-anxiety medications [53].

Thus, the treatment of insomnia in PD consists of a set of measures aimed at harmonising the emotional state, the autonomic nervous system and the management of PA and insomnia as syndromes. The key to successful therapy of sleep disorders in PD is a comprehensive approach, including, along with pharmacotherapy, a wide range of psychotherapeutic methods.

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# VERIFICATION OF ANGIOPROTECTIVE AND ANTI-INFLAMMATORY PROPERTIES OF VACCINIUM MYTILLUS, VACCINIUM ARCTOSTAPHYLOS IN EXPERIMENT

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## SUMMARY

The dental system is a complex mechanism that includes a number of connective tissue structures that have specific properties and perform a number of functions, in particular, protective. One of the main barrier elements of the oral cavity is the mucous membrane lining it, throughout its length, having a different morphological structure. The most frequently pathological process is the periodontal tissue, which consists of attached and non-attached gums, bone alveoli, cementum of the tooth root and periodontal ligament of the tooth. At present, all periodontal diseases are usually divided into inflammatory and primary dystrophic, while a number of authors have found that in its pure form, the dystrophic process is detected no more than 1–8% of all diseases and is characterized as a generalised process against the background of general somatic pathology. The frequency of occurrence of periodontal diseases varies from 60 to 85% in the working population, which determines the relevance of studying therapeutic measures aimed at their relief and is the purpose of this study.

**The aim of the study** was to investigate the angioprotective and anti-inflammatory properties of *Vaccinium mytillus*, *Vaccinium arctostaphylos* in experiment.

**Materials and methods.** In this experimental work, the authors developed a model of periodontal damage in experimental animals (Vistar rats, weight – 25–300 g) under the conditions of drug loading with chloral hydrate, in accordance with the Directive on the Protection of Vertebrate Animals of 2000 and extracts from the act of Local Ethical Committee. The model was created by inflicting a single injury with a sharp object in the projection of the interdental space in the frontal segment of the mandible. The proper pathological condition was recorded on the 5–7th day; the verification of the morphological changes in some of the animals was being made by fragmenting the frontal segment of the lower jaw, followed by a pathological and histological examination. Then, the control group of animals was treated applied gel, made of *Vaccinium mytillus*, *Vaccinium arctostaphylos* to stop the process for 2 weeks. For comparison, the main group was treated with a gel without the inclusion of a drug component. At the end of the course of conservative therapy, according to the design of the study, biopsy specimens were taken again in both groups to evaluate the results of the conservative therapy provided.

**Results.** According to the patho-histological study in the biopsy specimens of the damaged periodontium, the animals, revealed morphological disorders corresponding to chronic periodontal disease. At the stage of treatment in the control group, positive dynamics was noted both according to the clinical examination and after the pathological and histological examination of biopsy specimens in the comparison groups.

**Conclusions.** The obtained results indicate the presence of anti-inflammatory and angioprotective effect of medicament compositions based on *Vaccinium mytillus*, *Vaccinium arctostaphylos*, which will be further tested in clinical trials.

**KEYWORDS:** medicinal composition, modeling of the pathological process, biopsy specimens.

**CONFLICT OF INTEREST.** The authors declare no conflict of interest.

## ВЕРИФИКАЦИЯ АНГИОПРОТЕКТИВНЫХ И ПРОТИВОВОСПАЛИТЕЛЬНЫХ СВОЙСТВ VACCINIUM MYTILLUS, VACCINIUM ARCTOSTAPHYLOS В ЭКСПЕРИМЕНТЕ

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## РЕЗЮМЕ

Зубочелюстная система является сложным механизмом, включающим в себя ряд соединительнотканых структур, обладающих специфическими свойствами и выполняющими ряд функций, в частности защитной. Одним из основных барьерных элементов полости рта является выстилающая ее слизистая оболочка, на всем протяжении, имеющая различное морфологическое строение. Наиболее часто патологическому процессу подвергаются ткани пародонта, который состоит из прикрепленной и не прикрепленной десны, костной альвеолы, цемента корня зуба и периодонтальной связки зуба. В настоящее время все заболевания пародонта принято делить на воспалительные и первично-дистрофические, при этом рядом авторов, установлено, что в чистом виде дистрофический процесс выявляется не чаще 1–8% от всех заболеваний и характеризуется, как генерализованный процесс, на фоне общесоматической патологии. Частота встречаемости заболеваний пародонта варьирует от 60 до 85% у работоспособного населения, что определяет актуальность изучения терапевтических мероприятий, направленных на их купирование и является целью настоящего исследования.

**Целью исследования** было изучение ангиопротекторных и противовоспалительных свойств *Vaccinium myrtillus*, *Vaccinium arctostaphylos* в эксперименте.

**Материалы и методы.** В настоящей экспериментальной работе авторами разработана модель повреждения пародонта у животных, участвующих в эксперименте (крыс рода *Vistar*, весом 25–300 гр.) в условиях медикаментозной нагрузки препаратом хлоралгидрат, согласно директиве о защите позвоночных животных от 2000 г., и выписки из акта локального этического комитета ПМФИ № 10 от 02.03.2023 г. Модель создавалась посредством нанесения однократной травмы острым предметом в проекции межзубного пространства во фронтальном сегменте н/ч. Получение должного патологического состояния регистрировали на 5–7-е сутки, для верификации морфологических изменений у части животных, участвующих в эксперименте, забирали фрагмент тканей пародонта, путем фрагментации фронтального сегмента нижней челюсти, с последующим пато-гистологическим исследованием, после чего в течение 2-х недель ежедневно контрольной группе животных с целью купирования процесса наносили гель на основе *vaccinium myrtillus*, *vaccinium arctostaphylos*, для сравнения основной группе наносили гелевую основу без включения медикаментозного компонента. По окончании курса консервативной терапии согласно дизайну исследования проводили повторный забор биоптатов, как в контрольной, так и основных группах для оценки результатов оказываемой консервативной терапии.

**Результаты.** По данным патогистологического исследования в биоптатах поврежденного пародонта животных выявлены морфологические нарушения, соответствующие хроническому заболеванию пародонта. На этапе лечения в контрольной группе была отмечена положительная динамика как по данным клинического обследования, так и после патологоанатомического и гистологического исследования биоптатов в группах сравнения.

**Выводы.** Полученные результаты свидетельствуют о наличии противовоспалительного и ангиопротекторного действия лекарственных композиций на основе *Vaccinium myrtillus*, *Vaccinium arctostaphylos*, которые будут дополнительно протестированы в клинических испытаниях.

**КЛЮЧЕВЫЕ СЛОВА:** медикаментозная композиция, моделирование патологического процесса, биоптаты.

**КОНФЛИКТ ИНТЕРЕСОВ.** Авторы заявляют об отсутствии конфликта интересов.

## Introduction

*Vaccinium myrtillus*, *Vaccinium arctostaphylos* – common blueberry and Caucasian blueberry plants of the heather family (*Ericaceae*) are mostly distributed in mountainous areas, in coniferous, mixed and marshy forests [1]. The lack of wide distribution in the use of medicinal purposes is determined by the impossibility of cultivation. Despite this fact, since the 16th century, plants of the genus *Vaccinium* have been used as medicinal plants for such diseases as cholelithiasis, scurvy, tuberculosis, dysentery, as well as in the treatment of inflammatory diseases of the oropharynx with relevant evidence-based results of effectiveness [2, 3]. Relevant research today is the study of angioprotective properties associated with vascular ophthalmic pathology, vascular complications of diabetes mellitus and inflammatory periodontal diseases [4]. The chemical residue of medicinal plants varies depending on the part used. For fruits, the characteristic composition includes sugars (6–10%), citric, succinic, quinic, oxalic,

lactic and malic acids (1–1.3%), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances (0,14–0.69%), essential oil, tannins (12%), arbutin, flavonoids, triterpenoids, anthocyanin glycosides, as well as easily digestible manganese and iron compounds [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. For fruits, the characteristic composition includes sugars (6–10%), citric, succinic, quinic, oxalic, lactic and malic acids (1–1.3%), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances (0,14–0.69%), essential oil, tannins (12%), arbutin, flavonoids, triterpenoids, anthocyanin glycosides, as well as easily digestible manganese and iron compounds [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. For fruits, the characteristic composition includes sugars (6–10%), citric, succinic, quinic, oxalic, lactic and malic acids (1–1.3%), ascorbic acid, thiamine, riboflavin, nicotinic acid, carotenoids, pectin substances

(0,14–0,69%), essential oil, tannins (12%), arbutin, flavonoids, triterpenoids, anthocyanin glycosides, as well as easily digestible manganese and iron compounds [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. As well as easily digestible compounds of manganese and iron [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside. As well as easily digestible compounds of manganese and iron [5, 6]. The leaves, in turn, contain tannins, arbutin, flavonoids, phenolic glycoside.

The main elements with pharmacological activity are anthocyanides, which have high antioxidant activity, the ability to stabilize collagen molecules and accelerate its biosynthesis, reduce the permeability and fragility of the capillary link [7]. In addition, anthocyanides block the biosynthesis of pro-inflammatory mediators – histamine, prostaglandins and leukotrienes, thereby possessing anti-inflammatory activity. A number of scientists have identified antiallergic, antimicrobial, antiviral, antimutagenic, antiproliferative actions. Penarrola R., 1980 et al. [8], who studied microcirculation parameters such as vascular permeability, vascular wall thickness, linear blood flow velocity as in the experimental conditions, as well as in clinical practice, confirms the studied anti-inflammatory and angioprotective properties. Thus, in 47 patients with diagnosed venous insufficiency [9], blueberry extract contributed to the restoration of microcirculation, elimination of stagnation and stasis of blood in the vessels of the lower extremities.

Multiple therapeutic effects of the studied medicinal plant, in particular anti-inflammatory and angioprotective properties determined the purpose of this study: to study the properties and effectiveness of medicinal compositions based on *Vaccinium myrtillus*, *Vaccinium arctostaphylos* in inflammatory periodontal diseases in the experiment.

**The aim of the study** was to investigate the angioprotective and anti-inflammatory properties of *Vaccinium myrtillus*, *Vaccinium arctostaphylos* in experiment.

## Materials and methods

On the base of the PMFI vivarium, a branch of the Federal State Budgetary Educational Institution of Higher Education «VolgSMU» of the Ministry of HealthCare of the Russian Federation, 18 animals (white mice of the Vistar breed) were selected for the experiment, randomly divided into 3 experimental groups. Randomisation was performed by pulling alternately random numbers of animals. The weight of the animals did not exceed 300 g, keeping conditions: room temperature  $22 \pm 2$  °C, relative air humidity  $55 \pm 5$  °C. The maintenance of animals, the European Convention, 2002, and the local ethical committee No. 17 of February 10, 2023 carried out invasive manipulations in accordance with the Directive on the Protection of Vertebrate Animals. The division into groups was carried out as follows, in the first control group (n=6) the medicinal composition is represented by a gel without an active substance, second group (n=6) drug composition based on *Vaccinium myrtillus*, third group (n=6) drug com-

position based on *Vaccinium arctostaphylos*. Modeling of the pathological process (inflammatory periodontal disease) was carried out in all animals under the conditions of a drug load of chloral hydrate to achieve controlled short-term sedation. To obtain a pathological process in the periodontal tissues, the animals were subjected to a mechanical injury in the projection of the frontal incisors by inserting a 16G catheter into the interdental space. After infliction of injury for 7 days, dynamic monitoring of the progression of the pathological process was carried out. Next, the approbation of drug compositions and the application of the gel base for subsequent comparative analysis began. The application was performed once, daily, for 14 days.

## Results and discussion

In 18 animals, by 7 days of observation from the modeling of the pathological process, the phenomena of hyperemia, edema, formation of a periodontal pocket in the projection between the central incisors, a depth of  $3 \pm 0.06$  mm, with the presence of purulent detachable. The central incisors in 4 animals had mobility of the second degree (vestibulo-oral and mesio-distal directions), in 14 animals – the first degree (vestibulo-oral direction). The general condition of the animals did not suffer at the same time; the functional activity remained at the proper level, while there was difficulty in the usual volume in 4 animals, due to the mobility of the frontal group of teeth of the lower jaw. At the stages of approbation of medicinal compositions by the third day in the control group of animals, n=6 inflammatory phenomena remained in the same volume, in 2 cases progression of periodontitis was registered, with tooth mobility of the third degree (vestibulo-oral, mesio-distal, vertical). In the control groups, n=12, there was no progression of the pathological process. By the 7th day, in the animals in the main group, the phenomena of an inflammatory nature underwent a positive trend, the diameter of hyperemia decreased, and pathological mobility remained at the same level. In the main group, n=6 (second group), the periodontal pocket was reduced to 2 mm according to the metric measurement with a periodontal probe, the mobility of the frontal group of teeth remained the same. In the main group, n=6 (third group), the periodontal pocket was reduced to 2 mm according to the metric measurement with a periodontal probe,

By the 14th day in the control group of animals, the state of periodontal tissues was without pronounced dynamic changes, there was no discharge, while the mobility of the frontal group of teeth was in the 5th degree (vestibulo-oral, mesio-distal, vertical directions). In the animals, the main group n=12 has intact periodontium, a periodontal pocket up to 1 mm deep, and stable dentogingival attachment.

## Conclusions

The obtained results indicate the presence of anti-inflammatory and angioprotective effect of medicament compositions based on *Vaccinium myrtillus*, *Vaccinium arctostaphylos*, which will be further tested in clinical trials.

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# POINT STIMULATION WITH ESSENTIAL OILS IN COMPLEX TREATMENT OF LUMBOSACRAL DORSOPATHIES

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## SUMMARY

The material is devoted to the analysis of the main mechanisms and comparative assessment of the effectiveness of various options for the cutaneous use of essential oils in dorsopathies.

**Materials and methods.** 90 patients (women and men) with exacerbation of lumbosacral dorsopathy were selected. In the course of the study, along with neurological, psychological and electrophysiological analysis was carried out. The observed individuals were divided into three randomized groups, each of 30 people in which standard treatment was performed standard treatment. In addition to this, in the first two, main groups, a mixture of essential oils was used: in the 1st group by massaging the lumbosacral zone, in the 2nd – biopuncture, with its application to the area of segmental and distant acupuncture points. In the 3rd, control group, sesame oil was applied to the area of the same points as a placebo.

**Results and conclusion.** The results of the study confirmed the effectiveness of both types of use of essential oils, exceeding, at the level of reliability, the indicators of the control group. However, in the main groups, the rates of sustained analgesia varied, achieved on average after 7.2 procedures in the 1st and 5.5 in the 2nd group. In a similar proportion, the final intensity of pain also decreased – by 51.7 and 65 %, respectively, compared with the initial one. According to the delayed assessment performed after six months, exacerbations of the process in the control group were noted in a third of patients, while in the main groups they were observed in a comparably smaller number. Nevertheless, there are differences in the severity of periodically occurring algia: in the 2nd group they increased slightly, while in others they increased to a significantly greater extent. At the same time, the data of rheovasograms testified in favor of greater stability of the results in the 2nd group.

The noted advantage of biopuncture with essential oils can be explained by the cumulative effect inherent in the methods of reflexology. In addition, this technique, given the physiology, can be an addition to more aggressive types (classical acupuncture, electrical stimulation) of physical exposure.

**KEYWORDS:** dorsopathies, essential oils, reflexology, biopuncture, massage

**CONFLICT OF INTEREST.** The authors declare no conflict of interest.

## ТОЧЕЧНАЯ СТИМУЛЯЦИЯ ЭФИРНЫМИ МАСЛАМИ В КОМПЛЕКСНОМ ВОЗДЕЙСТВИИ ПРИ ПОЯСНИЧНО-КРЕСТЦОВЫХ ДОРСОПАТИЯХ

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## РЕЗЮМЕ

Работа посвящена анализу механизмов и оценки эффективности различных способов местного использования эфирных масел при вертеброгенной патологии.

**Материалы и методы.** Под наблюдением находилось 90 пациентов (38 женщин и 52 мужчины в возрасте от 40 до 75 лет с обострением дорсопатии на пояснично-крестцовом уровне. Наряду с неврологическим в работе был выполнен психологический (с применением анкетных методов) и электрофизиологический анализ, включающий термографию, реовазографию и ультразвуковую доплерографию сосудов голени и стоп. Было сформировано три группы из 30 пациентов каждая, в которых выполняли стандартное лечение. Дополнительно к этому в двух первых группах использовали смесь эфирных масел. В 1-й группе с применением данного состава выполняли массаж пояснично-крестцовой зоны, во 2-й использовали способ биопунктуры, т.е., нанося минимальные дозы смеси на проекции точек рефлексотерапии. В 3-ей, контрольной группе на область точек наносили кунжутное масло в качестве плацебо.

**Результаты и заключение.** В ходе работы подтверждена результативность обоих видов применения эфирных масел, достоверно превосходя в этом отношении показатели контроля. Однако при этом устойчивая анальгезия достигалась во 2-й группе достоверно ранее, чем в 1-й: в близкой к этому пропорции снижалась и итоговая интенсивность болевых ощущений. С другой стороны, в обеих группах использования масел прослеживалось сопоставимое улучшение зонального сосудистого обеспечения, подтвержденное электрофизиологически.

В ходе катamnестической оценки рецидивы дорсопатии в группе контроля были фиксированы у трети пациентов, тогда как в случае использования эфирных масел – в сопоставимо меньшем количестве. Тем не менее, в этих группах отмечены различия в выраженности периодически возникающих алгий: во 2-й группе они росли незначительно, тогда как в других – в большей степени. Кроме того, данные реовазограмм однозначно свидетельствовали в пользу большей устойчивости результатов именно во 2-й группе. Отмеченное преимущество биопунктуры эфирными маслами может быть объяснено кумулятивным эффектом, свойственным способам рефлексотерапии.

**КЛЮЧЕВЫЕ СЛОВА:** дорсопатии, эфирные масла, рефлексотерапия, биопунктура, массаж.

**КОНФЛИКТ ИНТЕРЕСОВ.** Авторы заявляют об отсутствии конфликта интересов.

## Introduction

The medical and social significance of dorsopathies, especially those formed at the lumbosacral level, is determined by the prevalence and protracted course of the process, leading in some cases to serious consequences. A distinctive feature of these conditions is also resistance to generally accepted therapeutic approaches [2,5,12,14], which explains the growing interest in other correction options [1,3]. The use of essential oils should be attributed to such, and insufficiently studied [6,10,15].

A standard technique for their topical application is massage, which contributes, among other effects, to blocking pain signals [7,13]. However, this effect is also inherent in other types of physical exposure [2,3], including biopuncture – an original technique for stimulating reflexology points with small doses of agents quoted by low-energy factors [1,9,11]. Moreover, in the case of such use of oils, it is possible to foresee an increase in the effectiveness of exposure due to the addition of several therapeutic links. In this regard, it seems relevant to compare the therapeutic capabilities of standard and biopuncture techniques for the use of essential oils, which led to the implementation of this study.

## Materials and methods

90 patients (38 women and 52 men aged 40 to 75 years) with exacerbation of dorsopathy at the lumbosacral level were under observation. The duration of the disease averaged 18.6 years, with a prevalence (in 2/3 of cases) in the range from 5 to 10 years. Most patients noted up to 2 exacerbations per year, with the duration of the latter more than two months.

The assessment of the patients' condition was based on the results of a comprehensive examination, including radiography and/or computed tomography and magnetic resonance imaging. In addition to neurological, psychological and electrophysiological analysis was performed. For the purpose of conditional objectification of the pain phenomenon, a visual-analogue scale (VAS) was used. To clarify the nature of changes in the mental sphere, the tests of the «Multilateral Personality Study» (MIL) and the «wellness-activity-mood» (WAM) tests were used. The complex of electrophysiological methods included thermography (AGA-782 device), rheovasography (Bioset-6001) and Doppler ultrasound of the vessels of the legs and feet (Acuson X300).

In the work, three groups were identified by randomization, 30 patients each. As a standard, the groups used a minimum amount of medication, magnetotherapy for the lumbosacral zone and the lower extremities area daily No. 10, as well as exercise therapy. In addition to this, in the first two

groups, a mixture of essential oils of Cayuput, Wintergreen, Rosemary shown in algia [11], dissolved in a base sesame oil, was used, observing standard WAMitary and hygienic requirements [13]. In the 1st comparison group, massage of the lumbosacral zone was performed using this composition. In the 2nd, main group, minimal doses of the mixture were applied to the projection of segmental and distant points of reflexology. In the 3rd control group, small doses of sesame oil were applied to the area of these points as a placebo. The treatment cycle in all groups included 10 procedures.

The effectiveness of treatment was assessed according to standard parameters, using parametric and nonparametric statistical methods within the framework of the Statistica for Windows v. 7 program. After 6 months, a follow-up analysis was performed.

## Results and discussion

In the examined group of patients, the prevalence of reflex over radicular syndromes was found in 64 versus 26 cases. At the same time, the vascular «pattern» of the process, noted in 73 (81 %) cases, was confirmed by the results of functional tests. In the course of assessing the intensity of algia using VAS, two equal subgroups with moderate and severe levels of pain were identified. As a result of clinical and psychological analysis, 68 (75 %) patients showed changes in the form of an affective component (in a third of cases) and astheno-neuroticism in other cases. In the first embodiment, the average MIL graph was distinguished by a slight peak (within 62 T-points) on the 1st scale and a rise on the right side of the profile, mainly in the 6th position. At the same time, the WAM test scores were moderately reduced (out of reliability with control) to an average of 47 points. In astheno-neurotic conditions, an increase in the MIL profile on the 1st scale (up to 73 T-points) was combined with a peak on the right side of the graph. There was also a decrease in the WAM test scores to 42–44 points.

In the process of thermography, foci of hyperthermia in the lumbosacral zone and hypothermia zones in the lower extremities, mainly on the side of pain, were revealed. According to rheovasography, the majority (78 %) of patients had a significant decrease in pulse blood filling of the distal parts of the lower extremities, with signs of tonic or spastic-atonie state of the arteries on the «affected» side. Doppler sonography confirmed the severity of shifts in the posterior tibial and arteries of the back of the foot in the form of a drop in volumetric blood flow in the vessels on the side of pain, with ambiguous changes in linear velocity. The noted

Table 1  
Effectiveness of the compared methods (in %)

| Groups                | Indicators              |                                                                                                    |             |      |               |      |               |     |
|-----------------------|-------------------------|----------------------------------------------------------------------------------------------------|-------------|------|---------------|------|---------------|-----|
|                       | Significant improvement |                                                                                                    | Improvement |      | Slight effect |      | Deterioration |     |
|                       | Abs.                    | %                                                                                                  | Abs.        | %    | Abs.          | %    | Aabs.         | %   |
| 1 (30)                | 9                       | 30                                                                                                 | 9           | 30   | 12            | 40   | -             | -   |
| 2 (30)                | 10                      | 33,3                                                                                               | 9           | 30   | 10            | 36,7 | 1             | 0,3 |
| 3 (30)                | 5                       | 16,6                                                                                               | 10          | 33,3 | 15            | 51,1 | -             | -   |
| Pearson test $\chi^2$ |                         | $\chi^2_{1,2}=1,71$ ( $p>0,05$ ) $\chi^2_{1,3}=10,1$ ( $p<0,05$ ) $\chi^2_{2,3}=10,2$ ( $p<0,05$ ) |             |      |               |      |               |     |

Note: the number of observations in parentheses.

Table 2  
Group pain regression ( $M\pm m$ )

| Groups | Pain level (cm) |                |
|--------|-----------------|----------------|
|        | Before          | After          |
| 1      | 5,6 $\pm$ 0,6   | 2,7 $\pm$ 0,4* |
| 2      | 5,6 $\pm$ 0,5   | 1,9 $\pm$ 0,3* |
| 3      | 5,7 $\pm$ 0,6   | 2,9 $\pm$ 0,4  |

Note: \* – reliability ( $p<0,05$ ) of changes in each of the indicators according to the Student's criterion.

Table 3  
Regression of the severity of thermoasymmetry in the region of the legs in groups ( $M\pm m$ )

| Groups | Severity of asymmetry ( $\Delta t^\circ C$ ) |                  |
|--------|----------------------------------------------|------------------|
|        | Before                                       | After            |
| 1 (28) | 1,38 $\pm$ 0,10                              | 0,79 $\pm$ 0,10* |
| 2 (26) | 1,37 $\pm$ 0,11                              | 0,77 $\pm$ 0,11* |
| 3 (28) | 1,37 $\pm$ 0,13                              | 1,18 $\pm$ 0,13  |

Note: in parentheses – the number of observations; \* – reliability ( $p<0,05$ ) of changes according to the Student's criterion.

Table 4  
Dynamics of lower leg rheovasograms in groups ( $M\pm m$ )

| Group   | Indicators           |                       |                    |                    |                     |                     |
|---------|----------------------|-----------------------|--------------------|--------------------|---------------------|---------------------|
|         | RI (Om)              |                       | DI                 |                    | VP (c)              |                     |
|         | Before               | After                 | Before             | After              | Before              | After               |
| 1 (24)  | 0,046 $\pm$<br>0,004 | 0,061 $\pm$<br>0,007* | 0,34 $\pm$<br>0,05 | 0,36 $\pm$<br>0,04 | 0,12 $\pm$<br>0,007 | 0,11 $\pm$<br>0,006 |
| 2 (25)  | 0,045 $\pm$<br>0,005 | 0,062 $\pm$<br>0,006* | 0,35 $\pm$<br>0,06 | 0,37 $\pm$<br>0,05 | 0,12 $\pm$<br>0,008 | 0,10 $\pm$<br>0,011 |
| 3 (22)  | 0,046 $\pm$<br>0,006 | 0,050 $\pm$<br>0,006  | 0,34 $\pm$<br>0,05 | 0,33 $\pm$<br>0,04 | 0,12 $\pm$<br>0,010 | 0,12 $\pm$<br>0,09  |
| Control | 0,07 $\pm$ 0,01      |                       | 0,39 $\pm$ 0,06    |                    | 0,09 $\pm$ 0,007    |                     |

Note: in parentheses – the number of observations; RI – rheographic index, DI – diastolic index, VP – pulse wave rise time; \* – reliability ( $p<0,05$ ) of changes according to the Student's criterion.

features provided a transition to the solution of the main task – comparing the effectiveness and therapeutic reliability of the compared technologies.

At the same time, the dynamics of the evaluated indicators confirmed the greater effectiveness of both types of use of essential oils in the form of a total «improvement of the condition» in 60 and 63.3 % of cases, respectively, significantly exceeding the control indicators (Table 1).

Reflex states, which make up the bulk of the study, turned out to be more «malleable» to the impact. In addition, biopuncture with essential oils, as the most physiological technique, showed significantly better results in the group of patients over 60 years of age, which to a certain extent agrees with the literature [15].

However, in the groups of oil use, the rates of sustained analgesia differed, achieved on average after 7.2 procedures in the 1st and 5.5 in the 2nd group. Taking into account the frequency of procedures dispensed every other day, a positive result was observed on average by 15 and 11 days of exposure. In a similar proportion, the total intensity of pain decreased – by 51.7 and 65 %, respectively, compared with the initial one (Table 2).

The noted advantage of biopuncture with oils in relieving pain, to a certain extent a psychological phenomenon, can be explained both by the actual irritation of the reflexology points and by the relaxing effect of low dosages of aromas.

In this regard, it becomes clear that the most favorable shifts in mental status were traced in response to the use of this technology. In particular, 68 % of patients indicated a decrease in affective tension and irritability – against 43 % and 33 % of cases, respectively, in the 1st and 3rd groups. Clinical characteristics were confirmed during testing: the analysis of the MIL test reflected a significant drop in the average peak on the 1st scale and a more favorable arrangement of the right positions of the graph only in the main group. In addition to this, there was a uniform increase in the average WAM indicators.

On the other hand, in both cases of the use of essential oils, similar changes in thermogram parameters were traced. In particular, the severity of thermoasymmetry at the level of the lower back decreased on average from 1.4 $\pm$ 0.08  $^\circ C$  to 0.75 $\pm$ 0.02  $^\circ C$ , within the limits of statistical significance, while in the placebo group – from 1.3 $\pm$ 0.07 to 1.0 $\pm$ 0.04  $^\circ C$  ( $p\geq 0,05$ ). A similar pattern was observed in the area of the lower extremities (Table 3).

In these two result groups, a comparable improvement in the rheographic characteristics (RI – reliably) of the legs was also revealed. On the contrary, in the control group, the persistence of «vascular» complaints was combined with minor changes in rheogram parameters (Table 4)

The results of Doppler ultrasound were consistent with the indicators of thermo- and rheographic examination, confirming the positive vascular effect of both groups of essential oil use.

Table 5  
Frequency of exacerbations of dorsopathy in groups

| Groups | Number of observations | Number of exacerbations |      |
|--------|------------------------|-------------------------|------|
|        |                        | Abs.                    | %    |
| 1      | 25                     | 6                       | 24   |
| 2      | 23                     | 5                       | 21,7 |
| 3      | 24                     | 8                       | 32   |

Table 6  
Dynamics of the level of pain in groups (M±m)

| Group | Level of algia (in cm)  |                  |
|-------|-------------------------|------------------|
|       | By the end of treatment | Six months later |
| 1     | 2,7 ±0,4                | 3,7±0,5          |
| 2     | 1,9±0,3                 | 2,3±0,4          |
| 3     | 2,9±0,4                 | 4,5±0,6*         |

Note: \* is the reliability ( $p < 0.05$ ) of changes according to the Student's criterion.

Thus, upon completion of treatment, the advantage of the options for using oils over placebo effects in achieving general clinical and vascular effects was established, however, with a significant superiority of the biopuncture scheme in the implementation of analgesic and psychotropic effects.

During the follow-up evaluation, recurrences of dorsopathy in the control group were noted in a third of patients, while in the case of the use of essential oils, there were comparably fewer (Table 5).

At the same time, differences in the severity of periodically occurring algia were revealed: in the main group, their intensity increased slightly, while in others to a greater extent, and in the control group, significantly (Table 6).

These data were consistent with the results of the assessment of the mental state of patients: in the biopuncture group, its satisfactory level was noted, while in more than half of the patients of other groups, complaints of the astheno-neurotic circle increased.

The shifts established in the course of electrophysiological analysis and, in particular, rheovasography and Doppler sonography unequivocally testified in favor of greater stability of indicators in the case of biopuncture with essential oils, even relative to the comparison group.

## Conclusion

Immediately upon completion of treatment, both options for the use of oils exceeded the placebo effect in achieving

the overall clinical and vascular effects, however, with a more distinct (reliable) analgesic and psychotropic effect of biopuncture. This advantage can be explained both by the actual irritation of the reflexology points and by the relaxing effect of low dosages of aromas.

The follow-up stage of the study also reflected differences in the degree of stability of the results achieved – both in terms of the level of recurrent pain and vascular support, which can be explained by the cumulative effect inherent in the methods of reflexology. In this case, the proposed method, which is distinguished by the addition of several therapeutic links, may be a component of programs for correcting the manifestations of dorsopathy. In addition, this technique, given the physiology, can be an addition to more aggressive types (classical acupuncture, electrical stimulation, etc.) of physical exposure.

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# DENTAL IMPLANTATION AFTER RECONSTRUCTION OF TOTAL AND SUBTOTAL DEFECTS OF THE UPPER AND LOWER JAWS

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## SUMMARY

Medical and social rehabilitation of patients with total jaw defects is an urgent surgical problem for maxillofacial surgeons. Cicatricial deformities, functional disorders of anatomical structures after resection are a difficult task for reconstructive surgery. It is impossible to achieve positive results without the use of digital technologies, a review of the methods of «digital dentistry» (CAD-CAM modeling and 3D printing) on clinical examples.

**The aim of the study** was to investigate the necessity of using digital technology in prosthetic patients with subtotal and total jawbone defects.

**Materials and methods.** The review provides examples of complex dental rehabilitation of patients with a detailed description of clinical and laboratory procedures, photographs and X-ray studies.

**Results.** An illustrative clinical example confirms the high value and significant role of computer simulation in complex clinical cases and situations. The presented technique made it possible to restore the former quality of life of patients, which indicates its high development today.

**Conclusions.** Clinical examples confirm the effectiveness of the use of digital dental technologies, prosthetics on implants in maxillofacial surgical dentistry. In the future, these methods will be improved through the introduction of new materials, workflow optimization and improved design accuracy using CAD-CAM and 3D modeling technologies.

**KEYWORDS:** total jaw defects, subtotal jaw defects, resection prosthesis, stereolithographic template, digital dentistry

**CONFLICT OF INTEREST.** The authors declare no conflict of interest.

## ДЕНТАЛЬНАЯ ИМПЛАНТАЦИЯ ПОСЛЕ РЕКОНСТРУКЦИИ ТОТАЛЬНЫХ И СУБТОТАЛЬНЫХ ДЕФЕКТОВ ВЕРХНЕЙ И НИЖНЕЙ ЧЕЛЮСТЕЙ

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## РЕЗЮМЕ

Медико-социальная реабилитация пациентов с тотальными дефектами челюсти является актуальной хирургической проблемой челюстно-лицевых хирургов. Рубцовые деформации, функциональные нарушения анатомических структур после резекции представляют собой сложную задачу для реконструктивной хирургии. Добиться положительных результатов без использования цифровых технологий невозможно, обзор методов «цифровой стоматологии» (CAD-CAM моделирование и 3D-печать) на клинических примерах.

**Цель работы:** изучение необходимости использования цифровых технологий у пациентов с протезированием с субтотальными и тотальными дефектами челюстной кости.

**Материалы и методы.** В обзоре приведены примеры комплексной стоматологической реабилитации пациентов с подробным описанием клинических и лабораторных манипуляций, фотографиями и рентгенологическими исследованиями.

**Результаты.** Наглядный клинический пример подтверждает высокую ценность и значимую роль компьютерного моделирования в сложных клинических случаях и ситуациях. Представленная методика позволила восстановить прежнее качество жизни пациентов, что свидетельствует об ее высоком развитии на сегодняшний день.

**Заключение.** Клинические примеры подтверждают эффективность использования цифровых стоматологических технологий, протезирования на имплантатах в челюстно-лицевой хирургической стоматологии. В будущем эти методы будут усовершенствованы за счет внедрения новых материалов, оптимизации рабочего процесса и повышения точности конструкций с использованием технологий CAD-CAM и 3D-моделирования.

**КЛЮЧЕВЫЕ СЛОВА:** тотальные дефекты челюсти, субтотальные дефекты челюсти, резекционный протез, стереолитографический шаблон, цифровая стоматология.

**КОНФЛИКТ ИНТЕРЕСОВ.** Авторы заявляют об отсутствии конфликта интересов.

## Introduction

Reconstruction of the dentition is an inseparable tandem of dentists (orthopedists), dental technicians and maxillofacial surgeons, as well as teams of related specialists using distant revascularizable flaps [1]. The logical conclusion of the successful restoration of the continuity of the jaw bones is the aesthetic and functional prosthetics in the projection of the missing dentition. To achieve the most beneficial result, as is known, according to the data of domestic and foreign authors, a number of conditions are required, in particular, the proper volume of soft tissue structures, osseointegration of dental implants, and other technical nuances required for prosthetics on an implant that is actually installed into the bone tissue [2,3]. The complexity of prosthetics for total and subtotal defects of the jaw bones lies in the difference in the morphological parameters of the connective tissue structures, in the prevailing majority of cases, after a total reconstruction, a number of corrective surgical interventions are required to achieve the goal. In addition, there are certain risks when installing dental implants, due to the type of transplanted bone structures, which corresponds to D1 according to the Mich classification [4]. In conditions of this type, dental implants with aggressive threads are required to ensure the absence of such phenomena as sliding, rotation and other types of movements [5]. This type of bone tissue requires special attention when installing implants, due to the high risk of its “overheating”, creation of compression and subsequent disturbances in blood supply, which is typical for the minimum content of spongy substance [6]. The failure of soft tissue structures is determined in view of the difference in morphology, the skin part, which appears in the oral cavity, does not lose its properties, and in addition to functional limitations, determines the aesthetic imbalance. Despite all the subtleties and existing risks, dental implantation with subsequent prosthetics is the only way to reconstruct total and subtotal postoperative defects of the jaw bones [7].

**The aim of the study** was to investigate the necessity of using digital technology in prosthetic patients with subtotal and total jawbone defects.

## Materials and methods

12 patients after subtotal resection of the lower jaw for bisphosphonate-induced osteonecrosis of the jaw bones underwent a rehabilitation stage using a revascularized fibular autograft, dental implantation and subsequent prosthetics in State Budgetary Health Institution of the Stavropol Territory «Stavropol Regional Clinical Hospital» from 2017 to 2023. Surgical interventions, fixation of personal and other data of patients were carried out after signing an informed voluntary consent to participate in a clinical trial. Patients with no consent to participate in it, somatic pathology in the acute stage were excluded from the study.

The stage of dental implantation was performed no earlier than 4 months after the reconstructive intervention using a fibular autograft. For the most accurate and predictable prosthetics, prototyping of future dentitions was performed using CAD-CAM computer technologies and 3D modeling. According to the virtual modeling protocol, all patients underwent prosthetics on at least 3 dental implants in two stages (immediate loading with a temporary orthopedic structure and “permanent” after 4–6 months). Navigational markings in the



Fig. 1. Patient K., condition after subtotal resection of the lower jaw in the anterior segment with a reconstructive-plastic component in the volume of restoration with an MB-flap and subsequent installation of dental implants for units, condition for 4 months



Fig. 2. Patient L., clinical stage of dental implantation in the projection of the autograft with the installation of gum formers

positioning of dental implants were used in all cases, which made it possible to set the exact installation angle and position relative to the load of the antagonistic dentoalveolar complex. For the accuracy of the additional visual research method in the volume of CBCT, a preliminary fixation was carried out at the time of the study in the oral cavity, a construction in the form of a wax template with radiopaque marks. Next, using three-dimensional modeling, a surgical stereolithographic template required for positioning dental implants was made.

## Results and discussion

48 dental implants were installed in 12 patients at the stage of restorative treatment, from 3 to 5 units in each case (Figure 1).

The absence of osseointegration was obtained in 2 patients, in one of whom 1 implant was explanted, in the second 2 implants. In both patients, this circumstance correlated with a critical increase in blood pressure in the early postoperative period, which caused increased bleeding and, as a result, suppuration of the postoperative wound with peri-implantitis phenomena that could not be stopped. The installation of gum formers was performed simultaneously with the actual stage of dental implantation in 11 patients (Figure 2).



Fig. 3. Patient A., final stage: fixed prosthodontic non-removable constructions

At the same time, the stage of prosthetics was carried out in all patients. Immediate loading with temporary structures allowed both to optimize the biomechanical balance of the dentition and to make the necessary adjustments to the aesthetic component of restoring the continuity of the dentition. At the end of the rehabilitation process, which consisted in restoring the continuity of the dentition with “temporary” structures, by the 6th month, all patients underwent fixation of permanent orthopedic structures (*Figure 3*).

## Conclusions

The use of navigation systems in dental implantation, as well as computer modeling in the conditions of reconstructive surgery after subtotal resections of the jaw bones, made it

possible to achieve osseointegration in 95 % of cases from the number of implants installed and to achieve the most favorable aesthetic indicators of prosthetics.

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## RECONSTRUCTIVE SURGERY OF POST-RESECTION DEFECTS OF THE UPPER JAW

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### SUMMARY

Post-resection defects of the upper jaw are one of the most difficult problems in surgery. They can occur after removal of tumors, trauma or infection, and can cause various functional and aesthetic problems in patients. Surgical reconstruction of the maxilla may require the use of bone grafts and/or implants, which may be ineffective or cause a number of complications in the absence of a reconstructive approach.

**The aim of the study** was to assess the efficacy and safety of surgical reconstruction of the upper jaw using modified individual plates and bone autografts.

**Materials and methods.** The study was conducted among 35 patients with post-resection defects of the upper jaw. All patients underwent surgical reconstruction using modified individual plates and revascularizable autografts, according to the division into 2 groups. Evaluation of the effectiveness of the reconstruction was carried out based on clinical data in the early and late postoperative periods.

**Results.** The use of revascularized flaps makes it possible to achieve an optimal long-term result with the absence of a large volume of foreign bodies in the recipient bed.

**Conclusions.** Reconstructive surgery using metal structures is fraught with a number of postoperative complications that require corrective manipulations and (or) a fundamentally different approach for repeated interventions. Currently, the gold alternative standard is the use of revascularized flaps, which allowed 16 patients to achieve a long-term stable result with the restoration of the continuity of the upper jaw, followed by prosthetics.

**KEYWORDS:** bone grafting, upper jaw, individual plates, revascularized autografts, post-bresection defects.

**CONFLICT OF INTEREST.** The authors declare no conflict of interest.

## РЕКОНСТРУКТИВНАЯ ХИРУРГИЯ ПОСТРЕЗЕКЦИОННЫХ ДЕФЕКТОВ ВЕРХНЕЙ ЧЕЛЮСТИ

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### РЕЗЮМЕ

Пострезекционные дефекты верхней челюсти являются одними из самых сложных проблем в хирургии. Они могут возникнуть после удаления опухолей, травмы или инфекции, и могут вызвать различные функциональные и эстетические проблемы у пациентов. Хирургическая реконструкция верхней челюсти может требовать использования костных трансплантатов и (или) имплантатов, которые могут быть неэффективными или вызвать ряд осложнений при отсутствии реконструктивного подхода.

**Цель.** Оценить эффективность и безопасности хирургической реконструкции верхней челюсти при помощи модифицированных индивидуальных пластин и костных аутоотрансплантатов.

**Материалы и методы** исследования. Исследование проводилось среди 35 пациентов с пострезекционными дефектами верхней челюсти. Все пациенты были подвергнуты хирургической реконструкции с использованием модифицированных индивидуальных пластин и реваскуляризируемы аутоотрансплантатов, согласно разделению на 2 группы. Оценка эффективности реконструкции проводилась на основе клинических данных в раннем и позднем послеоперационных периодах.

**Результаты.** Применение реваскуляризированных лоскутов позволяет достичь оптимального отдаленного результата с отсутствием большого объема инородных тел в реципиентном ложе.

**Выводы.** Реконструктивная хирургия с использованием металлоконструкций чревата рядом послеоперационных осложнений, требующих корректирующих манипуляций и (или) принципиально отличному подходу при повторных вмешательствах. Золотым альтернативным стандартом в настоящее время является применение реваскуляризуемых лоскутов, позволивших у 16 пациентов достигнуть отдаленного стабильного результата с восстановлением непрерывности верхней челюсти с последующим протезированием.

**КЛЮЧЕВЫЕ СЛОВА:** костная пластика, верхняя челюсть, индивидуальные пластины, реваскуляризуемые аутоотрансплантаты, пострезекционные дефекты.

**КОНФЛИКТ ИНТЕРЕСОВ.** Авторы заявляют об отсутствии конфликта интересов.

## Introduction

Modified individual plates – a reconstruction method, accompanied by computer modeling and printing of 3D plates, reproduced individually, according to the data of additional visual examination methods for each patient. These plates can be used to create a bone structure that accurately matches the anatomical shape and dimensions of the defect [1].

The use of modified individual plates for bone grafting of the upper jaw makes it possible to achieve high accuracy in matching the implant with the preserved bone structure [2]. At the same time, a number of clinicians noted that the manufacture of metal structures and their subsequent use in the long term leads to an unfavorable outcome in at least 30 % of cases [3]. Such a high percentage is primarily due to the lack of integration of the structure with connective tissue structures, which perceive it as a foreign body [4]. In addition, in the vast majority of cases, there are no suitable conditions for coating a metal structure, in particular, the proper volume of soft tissue structures [5]. To achieve an aesthetic result of prosthetics is also a time-consuming task. The introduction of dental implants becomes impossible and (or) a dubious process. A number of patients, in particular those of working age, are not ready for prosthetics with removable structures and, in striving for a highly aesthetic result, condemn the use of individual titanium implants [6]. To date, the «gold standard» in the reconstruction of post-resection defects of the upper jaw is the use of revascularized autografts [7]. Many opportunities for choosing a donor bed, a large volume of connective tissue and soft tissue structures determine in advance the expediency of choosing this surgical method in eliminating post-resection defects of the upper jaw [8].

**Thus, the aim of the study** is to assess the efficacy and safety of surgical reconstruction of the upper jaw using modified individual plates and bone autografts.

## Materials and methods

The study was conducted among 35 patients, aged 35 to 68 years, with post-resection defects of the upper jaw in State Budgetary Health Institution of the Stavropol Territory «Stavropol Regional Clinical Hospital» from 2015 to 2022. Patients were divided into 2 groups, in the main group 23 patients underwent defect reconstruction using individual plates, 12 patients in the control group using revascularized autografts. The exclusion criteria for patients were:

exacerbation of somatic pathology, the presence of vascular occlusion of the recipient and donor beds (occlusion over 30 %) according to X-ray endovascular angiography, lack of consent to participate in the study. All patients immediately before being included in the study signed an informed voluntary consent to participate in this study with permission to take photos, videos, as well as the publication of the results. In the preoperative period, additional visual methods were performed in both study groups, in particular MS CT with subsequent production of stereolithographic templates and X-ray endovascular angiography.

In the control group, according to the design of the study and the extent of the defect, a peroneal flap was chosen as an autograft, which allows volumetric defects of the upper jaw in the “double-barreled” model. In the main group, individual plates were made from a titanium alloy, according to the defect configuration, by reconstruction using computer modeling and subsequent 3D printing.

## Results and discussion

In the main group of patients intraoperatively, it was possible to achieve stability of the fabricated structure in all patients, the individual implant-prosthesis was overlapped with soft tissue structures without tension. At the same time, in the early postoperative period, on the 8th day, in 11 patients (50 %), the sutures diverged with the implant exposed. Further observation, taking into account conservative therapy, made it possible to stop the progression of the inflammatory process. At the end of the first month of observation in the main group, 5 patients had the implant exposed by 10 % of its volume with signs of infection of the surgical wound. Conservative management made it possible to stop the process in 3 patients. 2 patients underwent surgery for 2 months of postoperative follow-up with the removal of an individual prosthesis implant. In the control group, in the early postoperative period, 1 patient had a divergence of the sutures in the projection of the surgical wound. Under conditions of conservative administration, delayed sutures were applied, which made it possible to avoid purulent-inflammatory complications. In 2 patients, partial necrosis of the flap in the distal section was noted; under conditions of sparing necrectomy and soft tissue plastic surgery using free palatal grafts, flaps were saved. In the late postoperative period, the integration of the flap was achieved in all patients; at the end of 4 months of dynamic

follow-up, dental implantation was started in patients in the control group. In the control group, in the early postoperative period, 1 patient had a divergence of the sutures in the projection of the surgical wound. Under conditions of conservative administration, delayed sutures were applied, which made it possible to avoid purulent-inflammatory complications. In 2 patients, partial necrosis of the flap in the distal section was noted; under conditions of sparing necrectomy and soft tissue plastic surgery using free palatal grafts, flaps were saved. In the late postoperative period, the integration of the flap was achieved in all patients; at the end of 4 months of dynamic follow-up, dental implantation was started in patients in the control group. In the control group, in the early postoperative period, 1 patient had a divergence of the sutures in the projection of the surgical wound. Under conditions of conservative administration, delayed sutures were applied, which made it possible to avoid purulent-inflammatory complications. In 2 patients, partial necrosis of the flap in the distal section was noted; under conditions of sparing necrectomy and soft tissue plastic surgery using free palatal grafts, flaps were saved. In the late postoperative period, the integration of the flap was achieved in all patients; at the end of 4 months of dynamic follow-up, dental implantation was started in patients in the control group. which allowed to avoid purulent-inflammatory complications. In 2 patients, partial necrosis of the flap in the distal section was noted; under conditions of sparing necrectomy and soft tissue plastic surgery using free palatal grafts, flaps were saved. In the late postoperative period, the integration of the flap was achieved in all patients; at the end of 4 months of dynamic follow-up, dental implantation was started in patients in the control group. which allowed to avoid purulent-inflammatory complications. In 2 patients, partial necrosis of the flap in the distal section was noted; under conditions of sparing necrectomy and soft tissue plastic surgery using free palatal grafts, flaps were saved. In the late postoperative period, the integration of the flap was achieved in all patients; at the end of 4 months of dynamic follow-up, dental implantation was started in patients in the control group.

## Conclusions

The use of modified individual plates for bone grafting of the upper jaw in the elimination of post-resection defects is an effective technique to restore the structure and function of the upper jaw. Despite the fact that the results of studies indicate the high efficiency of this technique, the percentage of success of surgical intervention leaves much

to be desired. Compared with the use of autografts, the production of titanium implant prostheses is a faster and less labor-intensive method. In turn, the number of postoperative early and late complications, the impossibility of adequate dental prosthetics indicate the inappropriateness of the method. Reconstruction of maxillofacial defects remains a complex surgical procedure; the use of revascularized grafts is increasingly gaining momentum in the practice of maxillofacial surgeons and clearly determines the need for this method in patients with extended jaw bone defects.

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# Биоматериалы для управляемой регенерации

Изделия серии bioOST, bioPLATE и FibroMATRIX разработаны инженерами в соответствии с требованиями ведущих отечественных клиницистов. Это материалы для мягкой и костной пластики с управляемым поведением и надежным прогнозируемым результатом. Среди нашей линейки Вы сможете найти продукт, необходимый для решения индивидуальной клинической задачи любой сложности.



## bioOST

Костные гранулы с коллагеном  
XENOGRAFT Collagen

XCol-1-05 I 0.25-1.0 мм I 0.5 см<sup>3</sup>  
XCol-1-1 I 0.25-1.0 мм I 1.0 см<sup>3</sup>  
XCol-1-3 I 0.25-1.0 мм I 3.0 см<sup>3</sup>  
XCol-2-1 I 1.0-2.0 мм I 1.0 см<sup>3</sup>  
XCol-2-3 I 1.0-2.0 мм I 3.0 см<sup>3</sup>

Костные гранулы без коллагена  
XENOGRAFT Mineral

XMn-1-05 I 0.25-1.0 мм I 0.5 см<sup>3</sup>  
XMn-1-1 I 0.25-1.0 мм I 1.0 см<sup>3</sup>  
XMn-1-3 I 0.25-1.0 мм I 3.0 см<sup>3</sup>  
XMn-2-1 I 1.0-2.0 мм I 1.0 см<sup>3</sup>  
XMn-2-3 I 1.0-2.0 мм I 3.0 см<sup>3</sup>

Кортикальные гранулы  
XENOGRAFT Cortical  
XCr-1-05 I 0.5-1.0 мм I 0.5 см<sup>3</sup>  
XCr-1-1 I 0.5-1.0 мм I 1.0 см<sup>3</sup>

Губчатый блок CUBE Collagen  
Cb-10 I 20x10x10 мм

Кортикальная пластина  
CORTICAL Lamina  
Cl-25 I 25x25x1 мм

Кортикальная мембрана  
CORTICAL Membrane  
CM-20 I 25x20x0.2 мм

## bioPLATE

Мембрана bioPLATE Barrier  
MB-15 I 15x20 мм  
MB-25 I 25x25 мм  
MB-30 I 30x40 мм

Мембрана bioPLATE Contur  
MBC-15 I 15x20 мм  
MBC-25 I 25x25 мм  
MBC-30 I 30x40 мм

Коллагеновый 3D-матрикс  
FibroMATRIX  
FB-15 I 15x20 мм  
FB-30 I 30x40 мм  
FB-8 I 8 мм

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