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## IMPROVEMENT OF THE MEDICAL THERAPY REGIMENS FOR PATIENTS WITH II DEGREE GENERALIZED PERIODONTITIS AT THE STAGES OF CLOSED CURETTAGE AND COMPARISON OF THEIR EFFICACY

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Unmotivated use of antibiotics leads to the emergence of periodontopathogenic microorganisms strains resistant to them. It is necessary to develop modern regimens of drug therapy for treatment of inflammatory and dystrophic-inflammatory periodontal tissues diseases, which would not involve the local use of antibiotics. For medical treatment of patients with generalized II degree periodontitis, two regimens of drug therapy were suggested, one of which (No. 1) included local administration of an antibiotic and a non-steroidal anti-inflammatory drug in combination with oral administration of a proteolytic enzyme (serratiopeptidase) and the second regimen (No. 2) included only non-steroidal anti-inflammatory drug in combination with oral administration of a proteolytic enzyme. The regimens efficacy was assessed by the dynamics of hygienic and periodontal indices, as well as by the quantitative index dynamics of gum fluid and the presence of histamine and serotonin in it, as the inflammatory process mediators. Patients' recovery terms were also assessed. The performed clinical studies have proved the comparability of the drug therapy regimens 1 and 2 efficacy and permitted to recommend them for implementation in dental practice.

**Key words:** generalized periodontitis, closed curettage, gum fluid, histamine, serotonin.

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In recent years, the problem of antibiotic resistance, particularly in dental practice, has become increasingly urgent. Widespread availability, non-motivated use of antibiotic group drugs, irrational use in daily medical practice lead to emergence of new pathogenic microorganisms strains resistant to their effects [8, 9]. Therefore, modern dentists, researchers and practitioners are tasked to develop modern regimens of drug therapy for treatment of inflammatory and dystrophic-inflammatory periodontal tissues diseases, which would not involve the local use of antibiotics.

According to studies by Suda K.J., Calip G.S., Zhou J., 2019 [9] recommendations concerning the need for antibiotic prophylaxis before visiting a dentist for a specific category of patients, namely persons with pathological conditions that threaten with the subsequent onset and development of infectious endocarditis, were inappropriate. Estimating the studies results, the authors concluded that over 80% of the antibacterial drugs prescriptions for prevention of infectious complications before dental interventions were unreasonable, since most of the visits were either consultative or aimed at restoration of the teeth crown integrity. Dental procedures requiring the prevention of infectious endocarditis are all procedures including manipulations with gum or periapical tissues.

The list of analogous procedures also included manipulations including injury to the mucous membrane of the cavities and mouth. As a rule, antibiotic prophylaxis is prescribed to middle-aged and elderly people (55-72 years) before such dental manipulations. But despite this, dentists consider it necessary to prescribe antibiotics as a means of preventing secondary bacterial infection, regardless of the patients age [7, 8].

Given that the vast majority of patients with chronic generalized II degree periodontitis have concomitant pathology, mainly diseases of the gastrointestinal tract, cardiovascular, endocrine, kidney diseases, burdened allergic history, and combination of several somatic diseases, the rational antibiotic prevention should be carried out taking into account the side effects of the prescribed drugs (Volosovets T.M., 2013).

Since widespread antibiotics of penicillin, fluoroquinolone and linkosamide groups have quite a few of side effects, a number of authors consider it advisable to limit the local use of these drugs and only to prescribe them if necessary and after recovery study of the periodontal flora for sensitivity [1].

**The purpose** of the work was to study the developed regimens efficacy for medical treatment of patients with II degree generalized periodontitis at the stages of surgical treatment (closed curettage) and to perform a comparative efficacy analysis of the scheme, which included local antibiotic application according to the scheme, where non-steroidal anti-inflammatory drugs were used in combination with proteolytic enzymes.

**Materials and methods.** To perform this task, we examined and treated 69 patients with generalized II degree periodontitis within the age category from 35 to 60 years. The diagnosis was established according to the periodontal tissue diseases classification by M.F. Danilevsky (1994).

Diagnosis was verified based of conventional clinical and paraclinical examination methods with periodontal PI index (Russel, 1956), PMA (Parma, 1960), and gum recession assessment (P.D. Miller, 1985). Oral hygiene was assessed using the GI index (Green - Vermillion, 1964). The diagnosis was confirmed by radiography.

Patients whose periodontal pockets depth did not exceed 3.8 mm were involved in the study. In order to monitor the inflammatory process dynamics, the amount of gum fluid, histamine and serotonin content were performed before, after and during the surgery [1, 4, 5]. Patients were divided into 2 groups, depending on the medication regimens used during the surgery and postoperatively. Group I (main) included 37 patients. Group II (comparison) included 32 individuals. The course of the disease in patients of the both groups I and II was not burdened with excessive exudation and purulent discharge from periodontal pockets. The control group consisted of 20 persons with intact periodontal who consulted a dentist for uncomplicated caries treatment.

For the sake of the comparative analysis correctness in terms of the treatment regimens efficacy, the patients' groups homogeneity assessment was performed before the study and their comparability on demographic and clinical grounds was considered. All patients at phase I of generalized periodontitis treatment received a standard set of local therapies, which included the supra- and sub-gingival calculus removal, correction of butts, and other traumatic factors [2, 6].

Drug treatment included oral irrigation with antiseptic solutions, antibacterial therapy for periodontal pockets, anti-inflammatory and reparative treatment. To consolidate the effect of treatment, patients were offered closed curettage of periodontal pockets. At the time of surgery, patients in both Group I and Group II had an equivalent clinical picture of the disease. In order to prevent the systemic septicemia development and to avoid bacterial endocarditis, patients were prescribed prophylactic oral administration of clindamycin 60 minutes before the assigned surgery in the dose of 600 mg [2]. The operation of closed curettage for both groups was performed in the area of four incisors in the lower jaw according to the conventional method and under local anesthesia with a solution of articaine hydrochloride and irrigation with a warm antiseptic solution (0.05% solution of chlorhexidine bigluconate). Patients of the experimental (I) and the comparison (II) groups received postoperative drug therapy according to our suggested and developed regimens, which included oral administration of the serratiopeptidase drug [3]. Difference between the drug therapy regimens lied in the fact that Regimen 1 included local application of clindamycin phosphate-containing adhesive film, whereas Regimen 2 did not include local antibiotic use.

*Regimen No. 1*

At the first stage of the surgery:

1. Rinsing the periodontal pocket with a warm solution of antiseptic (0.5% aqueous solution of sodium mefenamate);
2. Instillation into periodontal pockets in the surgery intervention area (mefenamic acid, vinylin (Mefenate ointment) - 2.0; zinc oxide - 2.0), prepared immediately before use;
3. Application of an adhesive film containing clindamycin phosphate (Diplen-Denta K);
4. Prescription of serratiopeptidase for oral administration at the dose of 10 mg three times a day for 40 minutes before meals for 8 days.

The postoperative treatment of group II (comparison group) patients was performed according to the following scheme:

*Regimen No. 2*

1. Rinsing the periodontal pocket with a warm solution of antiseptic (0.05% solution of chlorhexidine bigluconate);
2. Instillation into periodontal pockets in the surgery intervention area (mefenamic acid, vinylin (Mefenate ointment) - 2.0; zinc oxide - 2.0), prepared immediately before use;
3. Adhesive bandage (Reso-pac);
4. Prescription of serratiopeptidase for oral administration at the dose of 10 mg three times a day for 40 minutes before meals for 8 days.

The control examination of groups I and II patients was carried out on the second day after the surgery. The term of the second surgery stage depends on the complaints and the clinical picture of the operation area.

At the second stage of surgery, the suggested regimens were supplemented with vitamin preparations (retinol acetate 3.44%, tocopherol acetate 10%) and reparative drugs (dental gel containing deproteinized calf blood hemoderivate). Patients in both groups I and II were given recommendations on oral hygiene. The treatment efficacy was assessed by the dynamics of hygienic and periodontal indices, as well as indices of the gum fluid dynamics and its histamine and serotonin content as biochemical markers of the presence and intensity of inflammatory process in the marginal periodontium and by terms of recovery.

**Results of the study and their discussion.** To assess the post-operative drug therapy regimens efficacy, clinical observations were made on the second day after the first intervention. Patients' complaints, periodontal dressing condition, presence or absence of exudation were assessed. Given that drug therapy regimens for the both groups included sodium mefenamate as an analgesic and anti-inflammatory agent and serratiopeptidase, which accelerates the penetration and activity of this drug, the vast majority of patients in both groups did not complain of pain. In addition, the adhesive bandage (Resopac) contains "Mirra" drug, which enhances internal energy metabolism, stimulates cell regeneration and blood microcirculation [6].

3 persons (8.1%) in group I and 2 persons (6.25%) in group II complained of mild pain. Slight edema and exudation were observed in 2 people in group I (5.4%) and in 1 person in group II (3.12%). In the absence of pronounced complaints of pain and a satisfactory clinical picture in the surgery site, the second surgery stage was performed on the third day after the first stage.

After the second stage of closed curettage, patients in the both groups I and II received drug therapy according to the treatment regimens selected for each group, respectively. Biochemical studies of gingival fluid on histamine and serotonin content to assess the intensity of the inflammatory process were performed on the second day (after stage I of the closed curettage) and on day 7 (after stage II). The study results on the dynamics of histamine and serotonin content in the gum fluid in groups I and II patients are presented in tables 1 and 2.

Table 1

**Dynamics of histamine content in gum fluid ( $\mu\text{g}/3 \text{ min}$ ) in patient groups I and II before treatment, on the third day after the first stage and on the seventh day after the second stage of closed curettage**

Group	Intact periodontium	Indices before treatment	On the 3rd day after stage I	On the 7th day after stage II
Group I (n=37)	-	*0.020±0.0009	* 0.026±0.0009	*0.012±0.0008
Group II (n=32)	-	*0.017±0.0006	*0.024±0.0009	*0.011±0.0007
Control group (n=20)	0.007±0.0005	-	-	-

Note: \* - reliability of differences in gum fluid histamine content prior to treatment and at different times after closed curettage ( $p \leq 0.05$ )

The data on the histamine content dynamics in the gum fluid before treatment, on the third and the seventh day after the surgery indicate an increase in the inflammatory process and exudative phenomena in periodontal tissues in response to traumatization. Moreover, on the second day, the histamine content significantly exceeds the respective indices before and within the shortest terms after the treatment.

The data on the serotonin content dynamics also confirm the increase in the inflammatory process intensity after the first stage of surgery, and the quantitative indices of serotonin content in the gum fluid significantly exceeded the quantitative indices of histamine (table 2), which may indicate the initiation of the inflammatory process in the marginal periodontium.

However, after the medical treatment, at the stage of healing, the severity of the inflammatory process decreased and quantitative indices of physiologically active substances, histamine and serotonin, in groups I and II were closer to those of intact periodontal patients.

Table 2

**Dynamics of serotonin content in gum fluid ( $\mu\text{g}/3 \text{ min}$ ) in patient groups I and II before treatment, on the third day after the first stage and on the seventh day after the second stage of closed curettage**

Group	Intact periodontium	Indices before treatment	On the 3rd day after stage I	On the 7th day after stage II
Group I (n=37)	-	* 0.024±0.0013	*0.034±0.0012	*0.013±0.0003
Group II (n=32)	-	*0.019±0.0002	*0.031±0.0007	*0.011±0.0004
Control group (n=20)	0.009±0.0006	-	-	-

Note: \* - reliability of differences in gum fluid serotonin content prior to treatment and at different times after closed curettage ( $p \leq 0.05$ )

The respective indices of histamine and serotonin content on the second day after stage I and on the 7th day after stage II in patients of both the main group and the comparison group had no significant difference between them, which may indicate the comparative efficacy of drug treatment regimens No. 1 and 2. After the first stage of closed curettage, which was accompanied by appropriate medical treatment, complications were not detected in either the main group or in the comparison group.

After the second stage of closed curettage, inflammatory exudation and pain in the surgical intervention site disappeared for 2-3 days. As a rule, on the third day the signs of a pronounced inflammatory process disappeared. The recovery terms had no reliable differences in both groups and amounted  $4.6 \pm 1.16$  days in patients of group I and  $4.1 \pm 1.12$  in patients of group II, respectively, as evidenced by the normalization of clinical indices presented in table 3.

**Dynamics of clinical indices in patient groups I and II before and within the shortest terms after treatment**

Indices	Control group (n=20)	Group 1 (n=37)		Group 2 (n=32)	
		Before treatment	After treatment	Before treatment	After treatment
IG	0.32±0.08	2.28±0.05	0.43±0.04*	2.33±0.04	0.36±0.08*
PI	0.1±0.002	2.25±0.15	0.67±0.06*	2.44±0.05	0.54±0.07*
Gingival bleeding index (SBI)	-	2.09±0.56	1.18±0.18*	1.82±0.37	1.01±0.21*
PMA index	6.31±0.61	34.89±1.38	8.10±2.18*	31.19±1.54	7.12±1.64*
Gum fluid amount	0.42±0.02	1.8±0.14*	0.8±0.05*	1.4±0.086	0.6±0.05*

Note: \* - reliability of differences in the indices values before and after the performed treatment ( $p \leq 0.05$ ).

In general, results of the above study are consistent with the data obtained by a number of researchers (Petrushanko T.O., Skrypnikov P.M., Litovchenko I.Y.u, Kolomiyets S.V. 2014), who studied the efficacy of the sticking patch containing "Mirra" drug. Studies were performed at the Ukrainian Medical Stomatological Academy According to the researchers, the patch eliminates congestive phenomena, improves microcirculation, provides optimal conditions for periodontal tissues regeneration and prevents possible complications in the postoperative period [6].

Efficacy assessment of the serratiopeptidase drug used in complex treatment regimens for patients with periodontal tissue pathology, especially after invasive intervention, also confirms the data obtained by the researchers (Voloshina L.I., Rybalov O.V., Skikevych M.G., Sokolova N.A. , 2014), who used this drug to treat lesions associated with impaired microcirculation, innervation and metabolism due to traumatic injuries of the oral mucosa in combination with infectious agents [3].

### Conclusions

1. Medical treatment regimens proposed and developed by us are quite efficient as evidenced by the positive dynamics of the gum fluid amount in patients in both I (main). and II (comparison) groups. The content of histamine and serotonin in the gum fluid of patients in the both groups also had positive dynamics and on the seventh day after the second stage of surgery was close to the quantitative indices of persons with intact periodontium. There were positive changes in the hygienic condition of the oral cavity, decrease in digital data of gingival bleeding indices, PMA, and the recovery terms reduced.

2. Drug regimens No. 1 and No. 2 are comparable in efficacy, because when applied, quantitative biochemical parameters, periodontal and hygiene indices both in group I (main). and in group II (comparison), showed no significant difference at both the operative and the recovery stages. The recovery terms in patients of groups I and II did not differ significantly.

3. Our study shows that in the absence of expressed patients' complaints and a satisfactory clinical picture of the surgery site, provided that drug therapy is properly selected, local use of antibiotics can be avoided to prevent the formation of pathogenic microflora antibiotic-resistant strains in patients' oral cavities.

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## Реферати

**УДОСКОНАЛЕННЯ СХЕМ  
МЕДИКАМЕНТОЗНОЇ ТЕРАПІЇ ПАЦІЄНТІВ  
ІЗ ГЕНЕРАЛІЗОВАНИМ ПАРОДОНТИТОМ  
ІІ СТУПЕНЯ НА ЕТАПАХ ПРОВЕДЕННЯ  
ЗАКРИТОГО КЮРЕТАЖУ  
ТА ПОРІВНЯННЯ ЇХ ЕФЕКТИВНОСТІ**

**Волосовець Т.М., Кравченко А.В.**

Немотивоване використання антибіотиків призводить до виникнення стійких до них штамів пародонтопатогенних мікроорганізмів. Необхідно розробити сучасні схеми медикаментозної терапії для лікування запальних та дистрофічно-запальних захворювань тканин пародонта, які не передбачали б місцевого застосування антибіотиків. Для медикаментозного лікування пацієнтів із генералізованим пародонтитом ІІ ступеня запропоновано два режими медикаментозної терапії, один з яких (№ 1) включав місцеве введення антибіотика та нестероїдного протизапального препарату у поєднанні з пероральним прийомом протеолітичного ферменту (серратіострептідази), а другий режим (№ 2) включав лише нестероїдні протизапальні препарати в поєднанні з пероральним прийомом протеолітичного ферменту. Ефективність режиму оцінювали за динамікою гігієнічних та пародонтальних показників, а також за кількісною динамікою індексу ясенної рідини та наявністю в ній гістаміну та серотоніну як медіаторів запального процесу. Також були оцінені терміни одужання пацієнтів. Проведені клінічні дослідження довели порівнянність ефективності режимів медикаментозної терапії 1 та 2 та дозволили рекомендувати їх для впровадження в стоматологічну практику.

**Ключові слова:** генералізований пародонтит, закритий кюретаж, ясенна рідина, гістамін, серотонін.

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**УСОВЕРШЕНСТВОВАНИЕ СХЕМ  
МЕДИКАМЕНТОЗНОЙ ТЕРАПИИ ПАЦИЕНТОВ  
С ГЕНЕРАЛИЗОВАННЫМ ПАРОДОНТИТОМ  
II СТЕПЕНИ НА ЭТАПАХ ПРОВЕДЕНИЯ ЗАКРЫТОГО  
КЮРЕТАЖА И СРАВНЕНИЯ  
ИХ ЭФФЕКТИВНОСТИ**

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Немотивированное использование антибиотиков приводит к возникновению устойчивых к ним штаммов пародонтопатогенных микроорганизмов. Необходимо разработать современные схемы медикаментозной терапии для лечения воспалительных и дистрофически-воспалительных заболеваний тканей пародонта, которые не предусматривали бы местного применения антибиотиков. Для медикаментозного лечения пациентов с генерализованным пародонтитом II степени предложены два режима медикаментозной терапии, один из которых (№ 1) включал местное введение антибиотика и нестероидных противовоспалительных препаратов в сочетании с пероральным приемом протеолитического фермента (серратіострептідазы), а второй режим (№ 2) включал только нестероидные противовоспалительные препараты в сочетании с пероральным приемом протеолитического фермента. Эффективность режима оценивали по динамике гигиенических и пародонтальных показателей, а также по количественной динамике индекса десневой жидкости и наличию в ней гистамина и серотонина как медиаторов воспалительного процесса. Также оценивались сроки выздоровления пациентов. Проведенные клинические исследования доказали сопоставимость эффективности режимов медикаментозной терапии 1 и 2 и позволили рекомендовать их для внедрения в стоматологическую практику.

**Ключевые слова:** генерализованный пародонтит, закрытый кюретаж, десневая жидкость, гистамин, серотонин.

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**METHODOLOGICAL PRINCIPLES OF THE CAUSAL-SYSTEM INJURY PROCESS  
MODELING**

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The method of causal systemic modeling of the natural relations of the traumatic process is developed on the basis of practical examinations of the archive of the Regional Bureau of Forensic Expertise (FE). Constructing the dependence of the trauma process of FE has been developed by combining traditional causal and modern systemic approaches. Causal systemic modeling of temporal pattern linkage (dependence) of the trauma process allowed: differentiate between causal and non-causal relationships of the full causal system; distinguish relationships: causal and effect (C-R) independent relationships (C-R), link states (LS); determine the relationships of the relationships of the relationships. The method of quasi-formal reproduction was developed in the plane of the text of the simulated objects of the traumatic process ensured the documentary recording of information about the relevant properties of the expert objects. Obtained objective system data on the properties of objects depending on the trauma process optimized forensic assessments of the role of objects and trauma events.

**Key words:** general methodology, common cause-system modeling, relevant forensic system objects, dependency verification, quasi-formal model reproduction.

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Forensic medicine is a multidisciplinary field of science and reflects the realized integration of various scientific knowledge, such as medicine, biology, chemistry, forensics and many other specialties. Forensic examination (FE) of relatively basic science of forensic medicine is the process of scientific and practical knowledge to apply scientific theories and concepts to address issues of law enforcement and the court. Logical and retrospective modeling operations are one of the current topical analytical trends in the