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STUDY OF THE POSSIBILITY OF USING CATGUT AS A CARRIER SUBSTANCE FOR ANTISEPTICS TO PREVENT RECOLONIZATION OF PATHOGENIC BACTERIA

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To achieve high efficiency in the treatment of patients with chronic generalized periodontitis, in recent years, therapeutic agents immobilized on natural or synthetic polymers, which are placed directly in the periodontal pocket, have been used. In this regard, the possibility of using catgut as a carrier substance for antiseptics to prevent recolonization of pathogenic bacteria was assessed. The studies were conducted on standard cultures of *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae* and *Porphyromonas gingivalis*. It was found that catgut has the ability to be saturated with antiseptic solutions, as evidenced by the long-term antibacterial effect of chlorhexidine and decasan on periodontal microorganisms. This allows us to significantly expand the scope of application of catgut as a stable complex for the transport of antiseptic substances.

Key words: generalized periodontitis, periodontal tabs, catgut, chlorhexidine, decasan.

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ВИВЧЕННЯ МОЖЛИВОСТІ ВИКОРИСТАННЯ КЕТГУТУ ЯК СУБСТАНЦІЇ-НОСІЯ ДЛЯ АНТИСЕПТИКІВ З МЕТОЮ ПОПЕРЕДЖЕННЯ РЕКОЛОНІЗАЦІЇ ПАТОГЕННИХ БАКТЕРІЙ

Для досягнення високої ефективності лікування пацієнтів із хронічним генералізованим пародонтитом в останні роки застосовуються лікувальні засоби, іммобілізовані на природних чи синтетичних полімерах, що розміщуються безпосередньо в пародонтальній кишені. У зв'язку з цим була здійснена оцінка можливості використання кетгуту як субстанції-носія для антисептиків із метою попередження реколонізації патогенних бактерій. Дослідження проводили на стандартних культурах *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae* та *Porphyromonas gingivalis*. Було встановлено, що кетгут має здатність насичуватись розчинами антисептиків, про що свідчить тривала антибактеріальна дія хлоргексидину та декасану щодо пародонтогенних мікроорганізмів. Саме це дозволяє значно розширити сферу застосування кетгуту як стабільного комплексу для переносу антисептичних речовин.

Ключові слова: генералізований пародонтит, пародонтальні вкладки, кетгут, хлоргексидин, декасан.

The study is a fragment of the research project "Development of pathogenetic prevention of pathological changes in the oral cavity of people with internal diseases", state registration No. 0121U108263.

Despite the significant successes of modern methods of treating periodontitis, and today the high frequency of progression of this inflammatory process and its complications remains an unresolved problem in dentistry [1]. The most important stage of treatment of patients with generalized periodontitis is professional oral hygiene. However, hardware and instrumental treatment of the pocket and root is not able to completely eliminate periodontal pathogens. To achieve high efficiency of scaling, general and local use of agents of different pharmacological groups is necessary, which would have a prolonged antimicrobial and fungicidal effect, not injure the surrounding tissues and promote their regeneration [2, 3].

To prevent re-infection of the pocket for many years, periodontologists have used the systemic administration of high doses of antibiotics to achieve the desired concentration of the drug in the gingival fluid. However, this tactic not only prevented the recolonization of pathogenic bacteria in the pocket, but also led to pathological changes in the gastrointestinal tract, allergic reactions and the emergence of resistant strains of bacteria.

In recent years, more and more researchers are considering the possibility of introducing therapeutic agents immobilized on natural or synthetic polymers directly into the periodontal pocket [5, 10]. Such carrier substances in the form of fibers, films, strips with medicinal agents fixed on them are able to locally release the active substance for a long time and slowly dissolve. However, the vast majority of known controlled-release systems contain antibiotics, the use of which on large segments of the dentition, although to a lesser extent, is still not devoid of the disadvantages inherent in systemic antibiotic therapy [6].

Due to the high price of these systems, the search for an alternative means for the effective treatment of patients with generalized periodontitis is extremely urgent. In this regard, we were interested in studying the effect on periodontal microflora of the system, where catgut acts as a carrier substance, and antiseptics such as Chlorhexidine and Decasan are immobilized on it as drugs.

The purpose of the study was to establish the possibility of using catgut as a carrier substance for antiseptics in order to prevent recolonization of periodontal pathogenic microorganisms in vitro.

Materials and methods. The study of prolonged antimicrobial activity of Chlorhexidine (form of release – 0.12 % solution of chlorhexidine bigluconate) and Decasan (form of release – decamethoxine 0.2 mg/ml) on the carrier substance catgut was conducted in the bacteriological laboratory of the municipal enterprise “Poltava Regional Clinical Hospital named after M.V. Sklifosovsky of the Poltava Regional Council”. As a carrier substance for immobilization of antimicrobial agents, catgut was used, which is an elastic thread of collagen material, which has a smooth surface, excellent plasticity, does not swell and independently resorbs after 7–12 days (loss of tensile strength up to 50 %). The study was conducted on standard cultures of *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae* and *Porphyromonas gingivalis*.

To determine the inhibitory activity of Chlorhexidine and Decasan, which were fixed on catgut, in the center of the cups with nutrient medium, on which standard cultures were inoculated, pieces (5 mm) of plain catgut (4/0) were placed, which were previously kept for 96 hours in a solution of chlorhexidine or decamethoxine with subsequent storage in a hermetically sealed container. The cups were placed in a thermostat at a temperature of 37°C. The duration and severity of the antibacterial activity of catgut-Chlorhexidine and catgut-Decasan complexes were studied by measuring the growth inhibition of the culture using the Hi-Antibiotic Zone Scale-C ruler. The growth inhibition zones around the catgut were measured after 24, 96 and 168 hours. Each study was performed in ten repetitions. The results of the studies were processed using the statistical software STATISTICA StatSoft with the calculation of the mean (M) and its error (m). Comparison of differences between the antimicrobial activity of catgut complexes with Chlorhexidine and Decasan against microorganisms was carried out using the Student's t-test. The value $p < 0.05$ was considered statistically significant.

Results of the study and their discussion. We have established that catgut has the ability to be saturated with antiseptic solutions, as evidenced by the long-term antibacterial effect of Chlorhexidine and Decasan on periodontal microorganisms. The study of bacterial growth inhibition zones around catgut segments as a carrier substance for the studied antiseptics for 168 hours allowed us to identify the sensitivity of test bacterial strains to the samples. No samples were found to have the absence of culture growth inhibition zones. However, it is necessary to pay attention to the unequal degree of the average value of the culture growth inhibition zones for catgut samples that were saturated with different antiseptics throughout the entire study period. The average values of the antimicrobial activity of antiseptics that were fixed on catgut against some periodontal microorganisms are given in Table 1.

Thanks to the results given in the table, it can be seen that catgut acts as a stable and effective carrier substance for local antiseptics, namely for such representatives as Chlorhexidine and Decasan. The best antimicrobial activity against periodontal test cultures *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae*, *Porphyromonas gingivalis* was demonstrated by local antiseptics in the first 24 hours of the study. The intensity of the inhibitory effect of both local antiseptics, which were fixed on the carrier substance, gradually decreases in the following periods of observation. However, the disinfecting effect against the specified periodontogenic microorganisms was somewhat more stable for catgut segments that were impregnated with chlorhexidine.

Thus, it can be seen that the samples of local antiseptics fixed on catgut showed high antimicrobial activity against the test culture of *Staphylococcus aureus* after 24 hours, namely the zones of growth inhibition were 25.5 ± 0.9 mm and 24.9 ± 0.7 mm for Chlorhexidine and Decasan, respectively. After 96 hours, these indicators decreased slightly, but antimicrobial activity continued to be maintained in both antiseptics. It was found that the sensitivity of strains *Staphylococcus aureus* to Chlorhexidine and Decasan after 24 and 96 hours did not differ significantly. After 168 hours of study, the catgut-Chlorhexidine complex was significantly more effective than Decasan, fixed on catgut, with the zones of growth inhibition being 21.8 ± 1.7 mm and 15.9 ± 1.3 mm, respectively.

Table 1

Antimicrobial activity of antiseptics fixed on catgut against some microorganisms

Growth retardation zone (mm)			
Staphylococcus aureus			
Complex Catgut+antiseptic	In 24 hours	In 96 hours	In 168 hours
Chlorhexidine	25.5±0.9	22.3±1.3	21.8±1.7
Decasan	24.9±0.7	20.5±1.1	15.9±1.3
			t=2.36; p<0.05
Streptococcus gallolyticus			
Complex Catgut+antiseptic	In 24 hours	In 96 hours	In 168 hours
Chlorhexidine	23.3±1.4	22.8±1.3	18.0±0.9
Decasan	22.0±1.1	17.4±0.8	16.5±1.2
		t=2.32; p<0.05	
Streptococcus agalactiae			
Complex Catgut+antiseptic	In 24 hours	In 96 hours	In 168 hours
Chlorhexidine	21.5±0.7	20.4±1.6	20.1±1.8
Decasan	20.5±1.6	19.4±1.8	15.8±2.1
			t=2.29; p<0.05
Porphyromonas gingivalis			
Complex Catgut+antiseptic	In 24 hours	In 96 hours	In 168 hours
Chlorhexidine	26.5±0.3	23.0±0.5	20.4±0.6
Decasan	22.5±1.3	21.3±1.5	16.8±1.5
			t=2.21; p<0.05

No significant difference in the effectiveness of the studied local antiseptics against the *Streptococcus gallolyticus* test culture was found after 24 hours of the study. After 96 hours of the study, significant differences in the sensitivity of the *Streptococcus gallolyticus* test culture to Chlorhexidine and Decasan were found ($t=2.32$; $p<0.05$). At the same time, the antimicrobial activity differed in favor of the catgut-Chlorhexidine complex. At a later time, after 168 hours, Chlorhexidine fixed on the catgut demonstrated slightly greater effectiveness against this periodontal test culture compared to the antimicrobial activity of the catgut-Decasan complex, but the difference between the indicators was not statistically significant.

The results of the studies revealed a high sensitivity of *Streptococcus agalactiae* to Chlorhexidine and Decasan, with which catgut segments were impregnated. At the same time, within 24 hours, the zones of inhibition of the growth of *Streptococcus agalactiae* in the nutrient medium for both local antiseptics did not differ significantly and were 21.5 ± 0.7 mm and 20.5 ± 1.6 mm, respectively. After 96 hours, local antiseptics continued to demonstrate high activity in inhibiting the growth of this pathogenic culture, and no significant difference in the indicators was established. However, after 168 hours, the size of the zone of inhibition of the growth of this culture around Chlorhexidine, which was impregnated with catgut, was 20.1 ± 1.8 mm, while the zone when using decasan was 15.8 ± 2.1 mm. That is, the catgut-Chlorhexidine complex demonstrated greater antimicrobial activity and a more stable effect.

Zones of lack of growth of *Porphyromonas gingivalis* in the nutrient medium were established for both local antiseptics that were included in the study, at all observation periods. It should be noted that the antimicrobial activity of the catgut-Chlorhexidine complex was slightly higher than that of Decasan, with which the carrier substance was impregnated, but after 24 hours the difference in bactericidal properties was insignificant. Statistically significant differences in the sensitivity of the test culture of *Porphyromonas gingivalis* to local antiseptics were not established even after 96 hours. We established a significant difference between the sizes of the zones of inhibition of the growth of the *Porphyromonas gingivalis* culture in the nutrient medium around the catgut segments impregnated with Chlorhexidine (20.4 ± 0.6 mm) and the catgut-Decasan complex (16.8 ± 1.5 mm) at a later time point of the study after 168 hours. This indicated a more stable activity of Chlorhexidine fixed on catgut as a carrier substance, compared to the material impregnated with Decasan.

Among antiseptics with a wide antimicrobial spectrum of action and high substantivity, it is necessary to note chlorhexidine and decamethoxin, the use of which in dental practice has already accumulated sufficient experience [4, 9]. The high antibacterial efficacy of these local antiseptics has been proven in both experimental and clinical studies [2, 7]. The action of chlorhexidine bigluconate is based on the absorption of its cell wall by most vegetative forms of gram-positive and gram-negative bacteria, yeast, dermatophytes and lipophilic viruses. Penetrating into the intracellular membranes of bacteria, it prevents oxygen consumption, which causes a decrease in ATP levels and leads to the death of bacterial cells [12]. Among the special additional properties of chlorhexidine, scientists highlight its ability to stably combine with the oral mucosa and enamel hydroxyapatite, as well as to be slowly released, maintaining an effective concentration [8].

Decamethoxin is a surfactant that is able to change the membrane permeability of a wide range of gram-positive and gram-negative, aerobic and anaerobic bacteria, leading to the destruction and death of the pathogen, which determines its bactericidal effect. In addition, decamethoxin has a bacteriostatic effect due to the inactivation of bacterial exotoxins and a decrease in the adhesion of microorganisms [1].

Typically, antiseptics for the treatment of periodontal patients are used in the form of sprays and solutions for rinsing the oral cavity, as well as toothpastes, gels and varnishes [8, 12]. However, a more effective, but also expensive option is to include them in the composition of controlled-release systems in the form of a gelatin chip [10]. However, the high cost of such long-acting agents makes their mass use impossible for the vast majority of patients with a generalized form of the inflammatory process in the periodontal tissues.

Our studies confirmed the high disinfecting effect of Chlorhexidine and Decasan against some periodontogenic microorganisms, which was established in previous works [1, 8, 12]. According to the data obtained by us, we can state the possibility of using catgut as a carrier substance for these local antiseptics in order to prolong the growth inhibition of test cultures *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae*, *Porphyromonas gingivalis*. Some advantage in the stability of antimicrobial activity in favor of Chlorhexidine compared to Decasan and some discrepancies with the results obtained by other researchers [7], in our opinion, may be associated with the different degree of saturation of catgut with these antiseptics. This assumption is a relevant issue that requires further in-depth study.

Conclusion

The possibility of using catgut as a carrier substance for antiseptics to prevent recolonization of pathogenic bacteria was considered from the standpoint of its targeted effect, reduction of antibiotic resistance and economic feasibility. During the study, it was found that catgut provides a gradual release of the antiseptic in the area of its implantation. This allows significantly expanding the scope of application of catgut as a stable complex for the transfer of antiseptic substances.

A more prolonged antibacterial effect was recorded against strains of *Staphylococcus aureus*, *Streptococcus gallolyticus*, *Streptococcus agalactiae* and *Porphyromonas gingivalis* in samples where chlorhexidine was immobilized on catgut. Thus, the use of catgut as a carrier substance for antiseptics leads to prolonged elimination of periodontal pathogenic microflora, which gives good prospects for this method in preventing recolonization of pathogenic bacteria after hardware and instrumental treatment of pockets and roots in patients with chronic generalized periodontitis.

In further studies, the clinical efficacy of catgut as a carrier substance for chlorhexidine in the complex treatment of patients with generalized periodontitis will be assessed. The issue of developing the most optimal treatment regimens for generalized periodontitis using catgut and other drugs immobilized on it for administration into periodontal pockets also seems important. It is also necessary to establish the efficacy of this technique in vivo depending on the severity of chronic generalized periodontitis.

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WELL-BEING, PHYSICAL ACTIVITY, AND RESPONSE TO PHYSICAL ACTIVITY IN PATIENTS WITH STAGE II HYPERTENSION AND FREQUENT EXTRASYSTOLES

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A total of 124 patients with stage II hypertension and frequent symptomatic extrasystoles aged 27 to 75 years were examined. They formed the main clinical sample of the study. Supraventricular extrasystoles (SVE) were recorded in 74 (59.7 %) patients, and ventricular (VE) in 50 (40.3 %) patients. It should be assumed that in patients with stage II hypertension and frequent extrasystole, the supraventricular variant is more common. Also, we examined 32 patients with stage II hypertension without any cardiac arrhythmias who were included in the comparison group. In addition to the mandatory examination methods, all patients were analyzed using visual analog scales of well-being and physical activity and an exercise test. Patients with frequent extrasystole, regardless of the location, have significantly ($p < 0.001$) worse well-being according to the visual analog scale with relatively preserved physical activity. According to the results of our analysis, in 73.4 % and 70.0 % of the subjects with SVE and VE respectively, the physical activity (walking upstairs 10 floors at usual pace), leads to the vanishing or significant reduction in the frequency of extrasystoles, which indicates a better functional state of the heart and the absence of severe cardiovascular pathology in those patients.

Key words: stage II arterial hypertension, supraventricular extrasystole, ventricular extrasystole, Holter ECG monitoring, exercise test.

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САМОПОЧУТТЯ, ФІЗИЧНА АКТИВНІСТЬ ТА РЕАКЦІЯ НА ФІЗИЧНЕ НАВАНТАЖЕННЯ У ПАЦІЄНТІВ З ГІПЕРТОНІЧНОЮ ХВОРОБОЮ ІІ СТАДІЇ ТА ЧАСТОЮ ЕКСТРАСИСТОЛІЄЮ

Було обстежено 124 пацієнти з гіпертонічною хворобою ІІ стадії та частою симптомною екстрасистолією віком від 27 до 75 років, які склали основний клінічний масив дослідження. Серед обстежених пацієнтів в 74 (59,7 %) осіб реєстрували суправентрикулярну і в 50 (40,3 %) – шлуночкову екстрасистолю. Слід вважати, що в пацієнтів з гіпертонічною хворобою і частою екстрасистолією суправентрикулярний варіант є більш частим варіантом екстрасистолії при ІІ стадії захворювання. Крім того нами обстежено 32 пацієнти із гіпертонічною хворобою ІІ стадії без будь-яких порушень серцевого ритму, які увійшли до групи порівняння. Усім пацієнтам, окрім обов'язкових методів обстеження, був проведений аналіз за візуальними аналоговими шкалами самопочуття та фізичної активності, а також проведена проба з фізичним навантаженням. Пацієнти з частою екстрасистолією, незалежно від топічного варіанту, мають достовірно ($p < 0.001$) гірше самопочуття згідно оцінки за візуальною аналоговою шкалою при відносно збереженій фізичній активності. За результатами нашого аналізу спостерігалось, що у 73,4 % і 70,0 % обстежених на тлі фізичного навантаження (ходьба на 10 поверхів у середньому темпі) реєстрували зникнення та суттєве зменшення частоти суправентрикулярної та шлуночкової екстрасистолії, що свідчить про кращий функціональний стан серця і відсутність важкої серцево-судинної патології у обстежених нами пацієнтів.

Ключові слова: артеріальна гіпертензія ІІ стадії, суправентрикулярна екстрасистолія, шлуночкова екстрасистолія, холтерівське моніторування ЕКГ, проба з фізичним навантаженням.

The study is a fragment of the research project "Cardiovascular remodeling, structural and functional state of the liver and kidneys and their relationship with cardiometabolic risk factors in patients with cardiac pathology and comorbidities. Possibilities of treatment optimization", state registration No. 0124U002036.

Arterial hypertension (AH) is one of the most common chronic diseases in the world, a non-communicable pandemic of the modern civilized world, and a major risk factor for cardiovascular disease and its complications [2, 5, 6]. Patients with arterial hypertension often have a variety of cardiac arrhythmias, the most common of which are extrasystole and atrial fibrillation. These arrhythmias can cause patients to experience subjective palpitations and/or interruptions in the heart region but