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EXPERIMENTAL SUBSTANTIATION OF THE USE OF THERAPEUTIC PROPHYLACTIC PASTE FOR PREVENTION OF COMPLICATIONS DURING ODONTOPREPARATION OF VITAL TEETH

Increased tooth sensitivity after preparation for non-removable orthopedic structures is a common problem in orthopedic dentistry. In many cases, it can contribute to morphofunctional changes in the hard tissues of the tooth and lead to various complications, with pulpitis and periodontitis being the most common. This article presents the results of a study of rat blood serum after experimental tooth trauma. An analysis of pulp inflammation markers was conducted, which demonstrated that the proposed therapeutic complex significantly reduces inflammatory reactions in the tooth pulp, increases nonspecific resistance and antioxidant status of the pulp in animals following odontopreparation. ***The aim of our study****. Experimental justification for the use of a complex of hyaluronic acid, bioflavonoids, and minerals to enhance the effectiveness of preventing complications after dental preparation for non-removable orthopedic structures. Investigate changes in pulp inflammation markers in the blood serum of experimental animals during dental preparation. Study the effect of the proposed complex on biochemical indicators in the blood serum of experimental animals.* ***Materials and methods.*** *The study was conducted on 48 sexually mature male Wistar rats weighing 220-270 g and aged 6-7 months. The animals were divided into 3 groups. The duration of the experiment was 21 days, after which the rats were euthanized under thiopental anesthesia (20 mg/kg) by bloodletting from the heart. Blood was collected to obtain serum. Serum catalase activity, alkaline phosphatase ALP, α2-macroglobulin, and alanine aminotransferase (ALT) were determined.* ***Results of the study and their discussion.*** *The study of alkaline phosphatase and alanine aminotransferase activity in the intact groups taken for analysis on the 7th and 21st day showed that these indicators were within the normal range and corresponded to data in the blood of rats presented in the literature sources.* ***Conclusions.*** *During the preparation of tooth crowns in experimental animals, pronounced inflammatory reactions develop in the traumatized pulp, which occur against the background of activation of the processes of oxidative stress (OS) with a characteristic phase course, accompanied by a significant increase in the concentration of inflammation markers in the blood serum. The proposed therapeutic and prophylactic complex effectively prevents established disturbances in the biochemical parameters of the blood serum of laboratory animals and is effective in preventing and preventing inflammatory processes in the pulp.*
Key words: *prevention, bioflavonoids, minerals, hyaluronic acid, dental preparation.*

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ЕКСПЕРИМЕНТАЛЬНЕ ОБҐРУНТУВАННЯ ЗАСТОСУВАННЯ ЛІКУВАЛЬНО ПРОФІЛАКТИЧНОЇ ПАСТИ ДЛЯ ПРОФІЛАКТИКИ УСКЛАДНЕНЬ ПРИ ОДОНТОПРЕПАРУВАННІ ВІТАЛЬНИХ ЗУБІВ

Підвищена чутливість зубів після процесу препарування під незнімні ортопедичні конструкції є досить поширеною проблемою ортопедичної стоматології. У великій кількості випадків це може сприяти процесу морфофункціональних змін в твердих тканинах зуба, а також є причиною різного роду ускладнень, з яких особливо поширеними є пульпіти і періодонтити. У статті представлені результати дослідження сироватки крові щурів при експериментальній травмі їх зубів. Проведено аналіз маркерів запалення пульпи, в результаті якого доведено, що запропонований комплекс значно знижує запальні реакції в пульпі зуба, підвищує неспецифічну резистентність і антиоксидантний статус пульпи зубів тварин в результаті одонтопрепарування. ***Мета нашої роботи.*** *Експериментальне обґрунтування застосування комплексу гіалуронової кислоти, біофлавоноїдів і мінералів для підвищення ефективності профілактики ускладнень після одонтопрепарування під незнімні ортопедичні конструкції. Дослідити зміни маркерів запалення пульпи зуба в сироватці крові експериментальних тварин при одонтопрепарировании. Вивчити вплив пропонованого комплексу на біохімічні показники в сироватці крові експериментальних тварин.* ***Матеріали і методи дослідження.*** *Дослідження проведено на 48 статевозрілих щурах-самцях лінії Вістар, масою 220-270 г, віком 6-7 місяців. Тварини*

були розподілені на 3 групи. Тривалість експерименту склала 21 днів, після закінчення яких щурів виводили з експерименту під тіопенталовим наркозом (20 мг/кг) шляхом кровопускання з серця. Збирали кров для отримання сироватки. У сироватці крові проводили визначення активності каталази, лужної фосфатази ЛФ, α2-макроглобуліну та аланінамінотрансферази АЛТ. ***Результати дослідження та їх обговорення.*** *Дослідження активності лужної фосфатази та аланінамінотрансферази в інтактних групах, які були взяті для аналізу на 7-му та 21-добу показали, що ці показники знаходились в межах норми та відповідали даним в крові щурів, що представлені в літературних джерелах.* ***Висновок.*** *При препаруванні коронок зубів у експериментальних тварин в травмованій пульпі розвиваються виражені запальні реакції, що протікають на тлі активації процесів перекисного стресу (ПС) з характерним фазовим перебігом, що супроводжується достовірним збільшенням концентрації маркерів запалення в сироватці крові. Пропонований лікувально-профілактичний комплекс ефективно запобігає встановлені порушення біохімічних показників в сироватці крові лабораторних тварин і ефективний для профілактики і запобігання запальних процесів в пульпі.*

Ключові слова: *профілактика, біофлавоноїди, мінерали, гіалуронова кислота, одонтопрепарування.*

Relevance. Increased tooth sensitivity after preparation for non-removable orthopedic structures is a fairly common problem in orthopedic dentistry. In many cases, this can contribute to morphofunctional changes in the hard tissues of the tooth and is also a cause of various complications, among which pulpitis and periodontitis are particularly common [11,12,18]. However, considering the aforementioned, it is considered justified to preserve the tooth pulp during treatment with non-removable orthopedic structures [9]. To protect the pulp of prepared abutment teeth for non-removable dental prostheses (NDP), temporary NDP structures fixed to the teeth with special hardening pastes are usually used during the laboratory stages of their manufacturing. However, practically all currently available hardening pastes serve mainly to fix temporary crowns on abutment teeth, without providing any significant therapeutic effect on the pulp traumatized to a greater or lesser extent during dental preparation. Considering the practically inevitable unfavorable effect of the tooth preparation procedure on the pulp's viability, it is obvious that materials for fixing temporary NDP should have the same properties as drugs recommended for the treatment of deep caries and pulpitis.

Considering the peculiarities of the pathogenesis of thermal and vibrational, mainly aseptic trauma of teeth during dental preparation, it should be assumed that the pharmacological action of such drugs should be complex.

The purpose of our work was to experimentally justify the use of a complex of hyaluronic acid, bioflavonoids, and minerals to enhance the effectiveness of preventing complications after dental preparation for non-removable orthopedic structures.

To achieve the stated goal, the following **tasks** were set**:**

1. Investigate changes in pulp inflammation markers in the blood serum of experimental animals during dental preparation.

2. Study the effect of the proposed complex on biochemical indicators in the blood serum of experimental animals.

Materials and methods. The study was conducted on 48 sexually mature male Wistar rats, weighing 220-270 g and aged 6-7 months. The animals were divided into three groups: Group 1 – intact control; Group 2 – traumatic injury; Group 3 – animals with traumatic injury receiving an application of the proposed therapeutic and prophylactic complex (TPC). Each group consisted of 16 animals, which were divided into subgroups (n=8) depending on the duration of removal from the experiment. The animals were removed from the experiment on the 7th and 21st days. The animals were kept under standard conditions and fed a standard vivarium diet. All research was conducted in accordance with modern international requirements and standards for humane treatment of animals (Council of Europe Convention of 18.03.1986 (Strasbourg); Helsinki Declaration 1975, revised and supplemented in 2 years, Law of Ukraine dated 21.02.2006 No. 3447-IV).

The duration of the experiment was 21 days, after which the rats were removed from the experiment under thiopental anesthesia (20 mg/kg) by bloodletting from the heart. Blood was collected to obtain serum. The serum was used to determine the activity of catalase, alkaline phosphatase ALP, α2-macroglobulin, and alanine aminotransferase ALT [1,3,4,5,6,11].

The therapeutic and prophylactic complex consisted of "Kvertgial" gel (SIA "Odessa Biotechnology", Ukraine), zinc oxide powder, HYDROCAL (calcium hydroxide powder; Cerkamed, Poland). The preparations were mixed ex tempore in equal proportions to obtain a homogeneous paste. The prepared paste was used to treat the exposed surface of the dentin and fix temporary crowns.

Results of the study and their discussion.

The study of alkaline phosphatase and alanine aminotransferase activity in intact groups taken for analysis on the 7th and 21st days showed (table 1) that these indicators were within the normal range

Table 1

The mean levels of alkaline phosphatase and alanine aminotransferase activity in the groups of experimental animals, M (SD)

Groups	Alkaline phosphatase, nmol/(sec×L)		Alanine aminotransferase (ALT), μmol/(h×mL)	
	7 day (n=24)	21 day (n=24)	7 day (n=24)	21 day (n=24)
1st group: intact control (n=8)	3352.8 (470.73)	3453.6 (387.22)	0.62 (0.068)	0.61 (0.057)
p_1	$p_1=0.539$		$p_1=0.526$	
2 group: traumatic injury (n=8)	6506.4 (1254.50)	6720.9 (1258.57)	0.60 (0.102)	1.5 (0.14)
p_1	$p_1=0.644$		$p_1<0.001$	
p_2	$p_2<0.001$	$p_2<0.001$	$p_2=0.474$	$p_2<0.001$
3 group: traumatic injury + therapeutic and prophylactic complex (n=8)	13780.6 (1467.33)	3509.9 (504.08)	0.67 (0.096)	0.69 (0.136)
p_1	$p_1<0.001$		$p_1=0.607$	
p_2	$p_2<0.001$	$p_2=0.695$	$p_2=0.372$	$p_2=0.018$
p_3	$p_3<0.001$	$p_3<0.001$	$p_3=0.259$	$p_3<0.001$

Notes. Differences between groups were analyzed using the Welch's t-test with Holm's corrections for multiple comparisons: p_1 – between day 7 and day 21; p_2 – compared to intact control; p_3 – compared to negative control (traumatic injury).

and corresponded to the data in the blood of rats presented in the literature sources [10, 13, 14].

In the traumatic injury group, the alkaline phosphatase activity was significantly increased ($p<0.001$) compared to the intact control group on both the 7th and 21st days of the study. An increase of almost two times was observed on the 7th day (3,153.53 (95 % CI 2,351.36–3,955.7) nmol/(sec×L) – 94.1 %), and the activity remained elevated on the 21st day ($p=0.644$).

A significant 4.11-fold increase in the level of ALP was observed in the 3rd experimental group on the 7th day compared to the 1st group ($p<0,001$).

At the same time, on the 21st day, its value significantly decreased ($p<0.001$): to 10,270.66 (95 % CI 9,320.47–11,220.85) nmol/(sec×L) – a decrease of 74.5 % – and reached a level that did not differ from the control values ($p=0.695$) during this period of the study.

When comparing the data on the 7th and 21st days of animal withdrawal from the experiment in groups 1 and 2, there was no tendency towards a decrease in the level of ALP. On the contrary, the levels of the indicator statistically non-significantly increased ($p>0,05$).

Comparison of the parameters in Group 3 – traumatic injury treated with the therapeutic-prophylactic complex and Group 2 – negative control (traumatic injury) showed that on the 7th day of the study, the level of ALP in Group 3 significantly exceeded that in Group 2, while on the 21st day it was significantly lower ($p<0.001$), indicating a positive effect of the proposed complex on the proteinase system of rat serum.

The values of alanine aminotransferase activity did not significantly differ in groups 2 and 3 from the control values of group 1 on day 7 ($p>0.05$), but significantly increased ($p<0.001$) in the traumatic injury group by 2.5 times (0.87 (95 % CI 0.78–0.96) μmol/(h×mL)) on day 21 of the study (see table 1). In the group with traumatic injury where the complex was applied, there was no significant increase in ALT activity on the 21st day of the study ($p=0.607$), while the values of the indicator in this period were statistically significantly higher ($p=0.018$) than those of the intact control, but there was no clinically significant difference since the indicators differed by 0.08 (95 % CI 0.02–0.15) μmol/(h×mL).

At the same time, the value of ALT in the 3rd group on day 21 of the study was 0.78 (95 % CI 0.69–0.87) μmol/(h×mL) or 52.9 % lower ($p<0.001$) compared to the results in the negative control group.

Based on the results obtained, the levels of activity of both enzymes decreased in the groups of rats that received a therapeutic and preventive complex after traumatic injury, especially on the 21st day. Moreover, the level of alkaline phosphatase activity did not differ significantly from the values in the intact group, and the activity of ALT was only increased by 13.7 % relative to the control. Therefore, it can be concluded that the use of hyaluronic acid in combination with quercetin and calcium hydroxide was effective.

The study of catalase activity, as a participant in the antioxidant system and an inhibitor of α2-macroglobulin, in intact groups taken for analysis at 7 and 21 days showed that these indicators were within

Table 2

Mean levels of catalase activity and α2-macroglobulin in experimental animal groups, M (SD)

Groups	Catalase, μmol/(s×L)		α2-macroglobulin, μmol/L	
	7 day (n=24)	21 day (n=24)	7 day (n=24)	21 day (n=24)
1st group: intact control (n=8)	4.9 (0.16)	4.8 (0.36)	9.8 (0.24)	9.7 (0.41)
p_1	p_1=0.438		p_1=0.563	
2 group: traumatic injury (n=8)	3.5 (0.67)	4.6 (0.47)	9.6 (1.07)	14.3 (3.79)
p_1	p_1<0.001		p_1<0.001	
p_2	p_2<0.001	p_2=0.189	p_2=0.612	p_2<0.001
3 group: traumatic injury + therapeutic and prophylactic complex (n=8)	4.7 (0.21)	4.8 (0.23)	9.7 (0.65)	9.8 (0.51)
p_1	p_1=0.438		p_1=0.824	
p_2	p_2=0.067	p_2=0.719	p_2=1.0	p_2=0.442
p_3	p_3<0.001	p_3=0.241	p_3=1.0	p_3<0.001

Notes. Differences between groups were analyzed using the Welch's t-test with Holm's corrections for multiple comparisons: p_1 – between day 7 and day 21; p_2 – compared to intact control; p_3 – compared to negative control (traumatic injury).

the normal range (table 2) and corresponded to the data presented in the reference literature [14].

It should be noted that the activity of catalase did not significantly change between the 7th and 21st day of observation in the 1st and 3rd study groups (*p>0.05*), and increased significantly by 1.13 (95 % CI 0.66–1.59) μmol/(s×L) or 32.4 % in the group with traumatic injury (*p<0.001*). On the 7th day of observation in the traumatic injury group, the activity of catalase was significantly lower (*p<0.001*) compared to the 1st and 3rd groups. At the same time, when using LPC, this indicator remained normal and did not differ from the intact control group. (*p=0.067*).

According to literature data, experimental acute periodontitis in rats also results in a decrease in catalase activity, and the use of the gel "Kvertulin" based on quercetin, inulin, and calcium citrate normalizes this indicator [8,15]. Since it is known that the flavonoid quercetin has antioxidant properties and its effective effect on catalase activity in patients has been proven [15], our results confirm the theory of its normalizing effect on the antioxidant system.

The activity of α2-macroglobulin did not significantly change on the 7th day compared to the intact control and the 3rd group in the case of traumatic injury (p>0.05). However, it increased by 47.9 % on the 21st day of the experiment (p<0.001), reaching 4.62 (95 % CI 2.75–6.48) μmol/L.

On day 21 of observation, the level of α2-macroglobulin in the group with traumatic injury and use of TPC did not differ from the intact control, while in the group with traumatic injury it significantly exceeded it. (p<0.001).

Both groups of rats where the proposed complex was used did not show significant changes over time (see table 2). The level of α2-macroglobulin, a protein with nonspecific inhibitory activity, was investigated in 2020 as part of proteomic analysis in volunteers with healthy, inflammatory, and necrotic pulp. An increase of this indicator by 2.33 times was demonstrated in the inflammatory pulp compared to healthy pulp [2], which explains our results regarding its increase in the bloodstream.

Conclusions:

1. During the preparation of tooth crowns in experimental animals, pronounced inflammatory reactions develop in the traumatized pulp, which occur against the background of activation of oxidative stress processes (OS) with a characteristic phased course, accompanied by a significant increase in the concentration of inflammation markers in the blood serum.

2. The proposed therapeutic and preventive complex effectively prevents the established biochemical abnormalities in the blood serum of laboratory animals and may be a useful measure in the prevention and management of pulp inflammation.

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