ЕКСПЕРИМЕНТАЛЬНО-ТЕОРЕТИЧНА СТОМАТОЛОГІЯ

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STUDY OF THE EFFECT OF THE DEVELOPED THERAPEUTIC AND PREVENTIVE COMPLEXES ON THE BIOCHEMICAL INDICES OF THE ORAL MUCOSA AND BLOOD SERUM OF RATS WITH TEETHING DISORDER AGAINST THE BACKGROUND OF A CARIOGENIC DIET

Teething disorder can cause accompanying pathological changes in the tissues of the oral cavity; therefore it is important to conduct experimental studies of this effect, as well as to study the effectiveness of preventive measures that can be used in such patients.
Objective: *to study the effect of the developed therapeutic-prophylactic complexes on the indices of urease and lysozyme of the mucous membrane of the oral cavity, alkaline phosphatase, elastase and catalase in the blood serum of rats with teething disorder against the background of a cariogenic diet.*
Methods. *Rats were divided into 8 groups. The animals of each group were given a cariogenic diet. The 1st (control) group consisted of 8 intact rats. A group 2 consisted of 10 rats with early teething. The 3rd group included 10 rats with early teething that received therapeutic-prophylactic complex (TPC) No1. A group 4 consisted of 10 rats with delayed teething (born to females that received antibiotics during pregnancy and lactation). The 5th group consisted of 11 rats with delayed teething (born to females that received antibiotics during pregnancy and lactation), which received TPC No2. The 6th group comprised rats that were modelled delayed teething (born to females that received Mercazolil during pregnancy and lactation). The 7th group included rats with delayed teething (born to females that received Mercazolil during pregnancy and lactation and TPC No. 2. The activity of urease and lysozyme was determined in the homogenates of the mucous membrane of the oral cavity. The activity of alkaline phosphatase (AL), lysozyme, elastase and catalase was determined in the blood serum.*
Results. *The use of TPC No. 1 in animals with early teething enabled to reduce the level of urease by 5.33 times and increase the level of lysozyme by 2.65 times in comparison with the 2nd group of rats. Catalase activity in the blood serum was 43.09% higher in rats of the group 5 that were treated with TPC No2 than in the animals of the group 4. In rats of the group 7, the level of catalase was higher by 50.82% than in animals of the group 6.*
Conclusions. *As a result of the study, it was established that the use of the proposed therapeutic and preventive complexes in rats with teething disorders against the background of a cariogenic diet allows normalizing the microbiocenosis in the mucous membranes of the oral cavity, antioxidant protection and the level of non-specific immunoresistance in the blood serum.*
Key words: *experiment, teething, biochemical indices of blood serum, biochemical indices of the mucous membrane of the oral cavity.*

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ДОСЛІДЖЕННЯ ВПЛИВУ РОЗРОБЛЕНИХ ЛІКУВАЛЬНО-ПРОФІЛАКТИЧНИХ КОМПЛЕКСІВ НА БІОХІМІЧНІ ПОКАЗНИКИ СЛИЗОВОЇ ОБОЛОНКИ ПОРОЖНИНИ РОТА ТА СИРОВАТКИ КРОВІ ЩУРІВ З ПОРУШЕННЯМ ТЕРМІНІВ ПРОРІЗУВАННЯ ЗУБІВ НА ТЛІ КАРІЄСОГЕННОГО РАЦІОНУ

Порушення прорізування зубів може викликати супутні патологічні зміни в тканинах порожнини рота, тому важливо провести експериментальні дослідження цього ефекту, а також вивчити ефективність профілактичних заходів, які можуть бути застосовані у таких пацієнтів. **Мета роботи.** *Вивчити вплив розроблених лікувально-профілактичних комплексів на показники уреази і лізоциму слизової оболонки порожнини рота, лужної фосфатази, еластази і каталази в сироватці крові щурів з порушенням прорізування зубів на тлі карієсогенної дієти.* **Матеріали і методи**. *Щурів* *розділили на 8 груп. Тваринам кожної групи давали карієсогенну дієту. 1-а (контрольна) група складалася з 8 інтактних щурів. 2-а група складалася з 10 щурів з раннім прорізуванням зубів. До 3-ї групи увійшли 10 щурів з раннім прорізуванням зубів, які отримували лікувально-профілактичний комплекс (ЛПК) № 1. До 4-ї групи увійшли 10 щурів із затримкою прорізування зубів (народилися від самок, які отримували антибіотики під час вагітності та лактації). 5-а група складалася з 11 щурів із затримкою прорізування зубів (народжених самками, які отримували антибіотики під час вагітності та лактації), які отримували ЛПК № 2. У 6-у групу увійшли щури, у яких моделювалося уповільнене прорізування зубів (народжені самками, які отримували мерказоліл під час вагітності та лактації). До 7-ї групи увійшли щури із затримкою прорізування зубів (народжені від самок, які отримували мерказоліл під час вагітності та лактації і ЛПК № 2). Активність уреази і лізоциму визначали в гомогенатах слизової оболонки порожнини рота. У сироватці крові визначали активність лужної фосфатази (ЛФ), лізоциму, еластази і каталази.* **Результати**. *Застосування ЛПК № 1 у тварин з раннім прорізуванням зубів дозволило знизити рівень уреази в 5,33 рази і підвищити рівень лізоциму в 2,65 рази в порівнянні з 2-ю групою щурів. Активність каталази в сироватці крові у щурів 5-ї групи, які отримували ЛПК № 2, була на 43,09 % вищою, ніж у тварин 4-ї групи. У щурів 7-ї групи рівень каталази був вище на 50,82 %, ніж у тварин 6-ї групи.* **Висновок.** *В результаті проведеного дослідження встановлено, що застосування пропонованих лікувально-профілактичних комплексів у щурів з порушеннями прорізування зубів на тлі карієсогенної дієти дозволяє нормалізувати мікробіоценоз слизових оболонок порожнини рота, антиоксидантний захист і рівень неспецифічної імунорезистентності в сироватці крові.*

Ключові слова: *експеримент, прорізування зубів, біохімічні показники сироватки крові, біохімічні показники слизової оболонки порожнини рота.*

The oral cavity performs important physiological functions and is constantly exposed to a number of negative exogenous factors [1, 2]. One of these factors is the ingress of pathogenic microorganisms, which can cause demineralization of hard tissues of the teeth, diseases of periodontal tissues and oral mucosa under the condition of impaired non-specific immunoresistance [3, 4, 5]. Considering the fact that delayed teething can cause accompanying pathological changes in the tissues of the oral cavity, it is important to conduct experimental studies of such an effect, as well as to study the effectiveness of preventive measures, which will make it possible to neutralize the negative impact of these factors [6, 7].

Thus, all of the above demonstrates the necessity and relevance of the study, which is aimed at studying the effect of the developed therapeutic and preventive complexes on indices of microbiocenosis in the mucous membrane of the oral cavity and biochemical indices of the blood serum in animals with teething delay against the background of a cariogenic diet.

The objective of the study: to study the effect of the developed therapeutic -preventive complexes on the indices of urease and lysozyme of the mucous membrane of the oral cavity, alkaline phosphatase, elastase and catalase in the blood serum of rats with teething delay against the background of the cariogenic diet.

Materials and methods. The experimental study was carried out in accordance with the requirements of the Law of Ukraine "On the Protection of Animals from Cruelty" (No. 1759-VI dated 15.12.2009) taking into account the rules of the European Convention on the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes.

In order to obtain animals with delayed and early teething, we used the models of teething delay developed by us [8]. For this purpose, 40 white female laboratory rats weighing 249-298 g, depending on the drugs used, were divided into 4 groups:

1. Intact rats that were on a vivarium diet;
2. Rats that received L-thyroxine at a dose of 10 mg/kg + vivarium diet;
3. Rats treated with antibiotics (cefoperazone 180 mg/kg – during pregnancy, amoxiclav 135 mg/kg – during lactation) + vivarium diet.
4. Rats that received Mercazolil – (20 mg/kg during pregnancy, 50 mg/kg during lactation) + vivarium diet.

All rats were kept under the standard conditions of the light regimen and food ration of the vivarium. Starting from the first day of drug administration, males were placed with females.

In the second group, rats received L-thyroxine (Berlin Chemie, Germany) orally at a dose of 10 mg/kg of body weight daily during pregnancy and lactation. In the rats born to this group of females, the molars of the upper and lower jaws erupted early.

In the 3rd group of animals, oral administration of antibiotics was carried out according to the following scheme: two courses of Cefoperazone (TOV "AVANT", Ukraine), which was administered orally in a dose of 180 mg/kg from the first day of the experiment for 6 days, the second course was carried out after an 8-day interval. After the 8-day interval, rats were given two courses of Amoxiclav (Lek, Slovenia) in a dose of 135 mg/kg. This period coincided with childbirth, that is, during lactation rats received two courses of amoxiclav. A total of four courses of antibiotic therapy were carried out with three intervals. In the rats born to this group of females, the eruption of upper and lower jaw molars was delayed.

In the 4th group, rats received the drug Mercazolil (Zdorovya Pharmaceutical Company LLC, Ukraine) orally. During pregnancy the rats received the drug in a dose of 20 mg/kg daily, during lactation the dose was increased to 50 mg/kg. In the rats born to this group of females, the eruption of upper and lower jaw molars was delayed.

Further experimental studies were carried out on 64 infant rats, which were born to them, in order to study the effect of the developed therapeutic – preventive complexes on the condition of the tissues of the oral cavity of the experimental animals against the background of the cariogenic diet. The rats were divided into 8 groups. The animals of each group were given a modified cariogenic diet by M.S. Bugaiova and S.A. Nikitin [9]. 1 (control) group consisted of 8 intact rats. A group 2 consisted of 10 rats with early teething (born to females that took L-thyroxine during pregnancy and lactation). The 3rd group included 10 rats with early teething (born to females that had L-thyroxine during pregnancy and lactation), which received treatment-preventive complex (TPC) No 1. A group 4 comprised 10 rats with delayed teething (born to females that took antibiotics during pregnancy and lactation). The 5th group consisted of 11 rats with delayed teething (born to females that had antibiotics during pregnancy and lactation), which received TPC No 2. The 6th group comprised rats that were modelled delayed teething (born to females that received Mercazolil during pregnancy and lactation). The 7th group included rats with delayed teething (born to females that took Mercazolil during pregnancy and lactation) that received TPC No 2.

Calcite gel was applied to the teeth of animals receiving TPC No 1 for 20 days. During the next 20 days, the rats were given applications of Biotrite Dent gel on their teeth with the simultaneous oral use of Biotrite Dent (400 mg/kg). After that the teeth of the rats were treated with the deep fluoridation system Ftorcalcit-E three times a day. For 30 days the rats receiving TPC No2 had applications with Calcite gel on their teeth, and the rats received Mineralol (1g/kg) orally. During the next 30 days, applications of Biotrite Dent gel were applied to the teeth with the simultaneous oral use of Biotrite Dent (400 mg/kg). During the entire experiment, the rats were orally treated with Lactiale Germina Forte (2 ml/kg).

60 days after the start of the experiment, the animals were euthanized under thiopental anesthesia (20 mg/kg).

The mucous membrane of the oral cavity was separated instrumentally. After that they were weighed and homogenized in porcelain mortars located on frozen cold accumulators. Homogenates with constant stirring were placed in the refrigerator for 30 minutes, and then they were centrifuged at 2500 rpm and +4°C for 15 min. The supernatant was transferred to test tubes and biochemical analysis was carried out. The urease and lysozyme activity was determined in the homogenates. The activity of alkaline phosphatase (AL), lysozyme, elastase, and catalase was determined in the blood serum [10, 11].

The STATISTICA 6.1 computer program was used for statistical processing of the results obtained to assess their reliability and measurement errors. A statistically significant difference between alternative quantitative signs with a distribution corresponding to the normal law was evaluated using the Student's t-test [12].

Study results. As a result of the conducted studies, an increase in the activity of urease in the mucous membrane against the background of the cariogenic diet was established in the rats with early and delayed teething. Thus, in animals of groups 2, 4, 6, this index was higher by 28 %, 36 %, and 52 %, respectively, compared to experimental animals of the group 1 (Table 1). At the same time, in the mucous membranes of the oral cavity, a decrease in lysozyme activity was observed in these groups by 42.67 %, 50.67 %, and 40.67 %, respectively, in comparison with the rats of the group 1. This indicates a decrease in non-specific immunoresistance in the mucous membrane of the oral cavity in animals with teething delay.

The use of TPC No1 in animals with early teething (the group 2) reduced the level of urease by 5.33 times and increased the level of lysozyme by 2.65 times compared to the group 2 rats. In experimental animals with delayed teething of the 5th group, which received TPC No2, the level of urease decreased by 85.29 % and the level of lysozyme increased by 2.65 times in comparison with the 4th group of rats. The use of TPC No2 in animals with delayed teething of the 7th group enabled to reduce the urease level by 78.95 % and increase the lysozyme level by 2.29 times in comparison with the 6th group of rats (Table 1). Such a change in the indices of urease and lysozyme in experimental animals that received the developed TPC indicates the normalization of microbiocenosis in the mucous membranes of the oral cavity.

The study results established that in the rats with early teething, which were on the cariogenic diet, the level of LF in the blood serum was significantly higher than in the rats of the group 1 by 16.25 %. There was also an increase in LF in the rats of the group 6 with delayed teething compared to animals of the group 1

Table 1

Indices of urease and lysozyme in the mucous membrane of the oral cavity of experimental animals

No.	Groups of rats	Urease activity, μ-cat/kg	Lysozyme activity, units/g
1.	Cariogenic diet n=8,	0.25±0.02	0.150±0.014
2.	Early teething ("L-thyroxine") + Cariogenic diet, n = 10	0.32±0.02 p<0.03	0.086±0.07 p<0.001
3.	Early eruption ("L-thyroxine") + Cariogenic diet + therapeutic and preventive complex No1, n = 10	0.06±0.005 p<0.001 p1<0.001	0.228±0.020 p<0.006 p 1<0.001
4.	Eruption delay ("Antibiotics") + Cariogenic ration, n =10	0.34±0.03 p<0.02	0.074±0.06 p<0.001
5.	Eruption delay ("Antibiotics") + Cariogenic ration + therapeutic and preventive complex No 2, n =11	0.05±0.004 p<0.001 p2<0.001	0.196±0.016 p<0.005 p2<0.001
6.	Eruption delay ("Mercazolil") + Cariogenic ration, n=7	0.38±0.03 p<0.004	0.089±0.007 p<0.002
7.	Eruption delay ("Mercazolil") + Cariogenic ration + therapeutic and preventive complex No 2, n =8	0.08±0.007 p<0.001 p3<0.001	0.204±0.018 p<0.03 p3<0.001

Notes: p – reliability of differences from the index of the group No 1;
p1 – reliability of differences from the index of the group No 2;
p2 – reliability of differences from the index of the group No 4;
p3 – reliability of differences from the index of the group No 6.

Table 2

Biochemical indices of blood serum of rats

No.	Groups of rats	LF activity, μ-cat/l	Activate elastases, μ-cat/l	Catalase activity, μ-cat/l	Lysozyme activity, units/l
1.	Cariogenic diet n=8,	6.40±0.35	189.64±14,12	0.278±0.021	0.050±0.0032
2.	Early eruption ("L-thyroxine") + Cariogenic diet, n =10	7.44±0.41 p<0.05	236.86±16.75 p<0.05	0.245±0.017 p>0.2	0.022±0.001 p<0.001
3.	Early eruption ("L-thyroxine") + Cariogenic ration +therapeutic and preventive complex No1, n =10	5.30±0.30 p<0.03 p1<0.001	110.26±8.20 p<0.001 p1<0.001	0.416±0.032 p<0.003 p1<0.001	0.071±0.003 p<0.001 p1<0.001
4.	Eruption delay ("Antibiotics") + Cariogenic diet, n =10	7.22±0.51 p>0.2	244.38±15.48 p<0.02	0.311±0.020 p>0.3	0.025 ± 0.001 p<0.001
5.	Eruption delay ("Antibiotics") + Cariogenic diet + therapeutic-preventive complex No2, n =11	5.05±0.34 p<0.01	129.45±8.42 p<0.002 p2<0.001	0.445±0.032 p<0.001 p2<0.002	0.068±0.003 p<0.001 p2<0.001
6.	Eruption delay ("Mercazolil") + Cariogenic diet, n =7	7.48±0.36 p<0.05	196.02±11.01 p>0.07	0.305±0.024 p>0.04	0.020±0.002 p<0.001
7.	Eruption delay ("Mercazolil") + Cariogenic diet + therapeutic-preventive complex No2, n =8	5.01±0.36 p<0.02 p3<0.001	125.86±9.32 p<0.002 p3<0.001	0.460±0.037 p<0.001 p3<0.004	0.072±0.003 p<0.001 p3<0.001

Notes:p – reliability of differences from the index of the group No 1;
p1 – reliability of differences from the index of the group No2;
p2 – reliability of differences from the index of the group No 4;
p3 – reliability of differences from the index of the group No 6.

by 16.88 %. Such an increase in the activity of LF in pregnant groups may be associated with a metabolic disorder of the bone tissue. The appointment of TPC No 1 in the rats of the group 3 allowed reducing the level of LF reliably in comparison with animals of the group 2 by 28.76 %. The appointment of TPC No 2 in rats of the group 5 made it possible to reduce the level of LF reliably by 30.06% in comparison with animals of the group 4 (Table 2).

In the rats of the groups 2 and 4 with delay of teething, which consumed the cariogenic diet, an increase in elastase in the blood serum was established in comparison with the indices of experimental animals of the group 1 by 24.9 %, 28.87 %, respectively. Such a change in elastase activity is a sign of systemic inflammation. In the rats with early eruption of the teeth of the group 3, which were on the cariogenic diet and used TPC No 1, a decrease in elastase by 53.45 % was found compared to animals of the group 2. A decrease in elastase was also noted when using TPC No 2. Thus, in the rats of the group 5, which were treated with TPC No 2, elastase activity in the blood serum was 47.03 % lower than in animals of the group 4 (Table 2).

Studies of the catalase level in the blood serum of experimental animals with delay of teething of the groups 2, 4 and 6 under the conditions of consumption of the cariogenic diet indicate the suppression of the antioxidant defence of the body of rats of these groups. The use of TPC No1 in animals of the group 3 enabled to normalize antioxidant protection, which was confirmed by an increase in catalase activity by 69.8 % compared to the indices of animals in the group 2. Normalization of the catalase level was also noted in animals treated with TPC No 2. Thus, in the rats of the group 5, which were treated with TPC No2, the catalase activity in the blood serum was 43.09 % higher than in animals of the group 4. In the rats of the group 7, the level of catalase was 50.82 % higher than in animals of the group 6 (Table 2).

As a result of the conducted studies, it was established that the level of non-specific immunoresistance of the blood serum in rats against the background of the cariogenic diet with early and delayed teething was confirmed by a decrease in the lysozyme activity. Thus, in animals of the groups 2, 4, 6, this index was lower by 56 %, 50 %, and 60 %, respectively, compared to experimental animals of the group 1 (Table 2). An increase in the lysozyme activity by 3.23 times compared to animals of the group 2 was found in rats with early teething of the group 3, which were on the cariogenic diet and were treated with TPC No1. An increase in lysozyme was also noted when using TPC No2. Thus, in the rats of the group 5, which were treated with TPC No2, the activity of lysozyme in the blood serum was 2.72 times higher than in those of the group 4. The activity of lysozyme in the blood serum was 3.6 times higher in the rats of the group 7 that were treated with TPC No 2 than in animals of the group 6.

Conclusions

1. As a result of the study, it was found that the use of the proposed TPC No1 and TPC No2 in rats with early and delay teething against the background of the cariogenic diet allows normalizing microbiocenosis in the mucous membranes of the oral cavity.

2. It has been proven that the use of the proposed TPC No 1 and TPC No2 enables to normalize antioxidant protection and the level of non-specific immunoresistance in the blood serum of rats with early and delay teething against the background of the cariogenic diet.

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