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STUDY OF MARKERS OF ANTIOXIDANT PROTECTION OF THE ORAL CAVITY IN THE ORAL FLUID OF PATIENTS WITH PERI-IMPLANTITIS AGAINST THE BACKGROUND OF THE TREATMENT AND PREVENTION COMPLEX

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The study was devoted to researching the effect of the treatment and preventive complex on biochemical markers of the antioxidant system in the oral fluid of patients with peri-implantitis. 40 patients with peri-implantitis aged between 25 and 55 years took part in the research. In the oral fluid of patients, the indicator of antioxidant protection of the oral cavity was determined. The therapeutic and prophylactic complex led to a substantial elevation in the antioxidant-prooxidant index, exceeding the levels found in somatically healthy patients after six months of treatment. This antioxidant-prooxidant index elevation suggests a restoration and amplification of non-specific oral cavity resistance, emphasizing the complex's potential to sustain long-term antioxidant defense in patients with peri-implantitis amid concomitant conditions like periodontitis and atherosclerosis.

Key words: oral fluid, health of the oral cavity, implants, treatment and prevention complex, adult patients.

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ДОСЛІДЖЕННЯ МАРКЕРІВ АНТИОКСИДАНТНОГО ЗАХИСТУ РОТОВОЇ ПОРОЖНИНИ У РОТОВІЙ РІДИНІ ПАЦІЄНТІВ З ПЕРИІМПЛАНТИТАМИ НА ТЛІ ЗАСТОСУВАННЯ ЛІКУВАЛЬНО-ПРОФІЛАКТИЧНОГО КОМПЛЕКСУ

Дослідження було присвячено вивченню впливу лікувально-профілактичного комплексу на біохімічні маркери антиоксидантної системи в ротовій рідині пацієнтів з періімплантитом. У дослідженні взяли участь 40 пацієнтів з періімплантитом у віці від 25 до 55 років. У ротовій рідині пацієнтів визначали показники антиоксидантного захисту порожнини рота. Лікувально-профілактичний комплекс призвів до суттєвого підвищення антиоксидантно-прооксидантного індексу, що перевищував рівні, виявлені у соматично здорових пацієнтів через шість місяців лікування. Таке підвищення антиоксидантно-прооксидантного індексу свідчить про відновлення та посилення неспецифічної резистентності порожнини рота, що підкреслює потенціал комплексу для підтримання тривалого антиоксидантного захисту у пацієнтів з періімплантитом.

Ключові слова: ротова рідина, здоров'я порожнини рота, імпланти, лікувально-профілактичний комплекс, дорослі пацієнти.

The work is a fragment of the research project “Improving the prediction of the occurrence and course of dental caries and periodontal disease, schemes for their prevention and treatment”, state registration No. 0121U114672.

Peri-implantitis is a progressive inflammatory disease affecting the tissues surrounding dental implants, characterized by the destruction of supporting bone and potential implant failure [6]. The condition has emerged as a significant clinical challenge in implant dentistry due to its complex etiology involving microbial colonization, host immune responses, and various systemic factors [7, 10]. Despite advances in implant technology and surgical techniques, the prevalence of peri-implantitis remains high, necessitating a deeper understanding of its pathogenesis and the development of more effective treatment strategies [9, 11].

Oxidative stress plays a pivotal role in the pathogenesis of peri-implantitis, where an imbalance between pro-oxidant and antioxidant systems leads to tissue damage and inflammation [8]. Reactive oxygen species generated during inflammatory responses and microbial metabolism can overwhelm the local antioxidant defenses of the oral cavity, exacerbating tissue destruction [12]. Catalase, a key antioxidant enzyme, mitigates oxidative stress by decomposing hydrogen peroxide, a harmful by-product of cellular metabolism and bacterial activity. Enhancing the activity of catalase and other antioxidant mechanisms may therefore represent a promising therapeutic avenue.

Current treatment protocols for peri-implantitis primarily focus on mechanical debridement and antimicrobial interventions to reduce bacterial load [4, 5]. However, these approaches may not adequately address the underlying oxidative stress and may be less effective in patients with systemic conditions such as

periodontitis and atherosclerosis, which are known to exacerbate inflammatory responses [3, 7]. Moreover, the interrelationship between periodontal disease, systemic health, and peri-implantitis underscores the need for comprehensive treatment modalities that consider both local and systemic factors [6, 11].

Recent studies have suggested that patients with peri-implantitis exhibit altered levels of oral fluid biomarkers associated with oxidative stress and inflammation [9]. Despite this knowledge, there is a paucity of research investigating therapeutic interventions aimed at modulating the antioxidant-prooxidant balance in the oral environment. Addressing this gap could lead to improved clinical outcomes by enhancing the body's natural defense mechanisms against oxidative damage.

The present study seeks to explore the effects of a therapeutic and preventive complex that includes antioxidants, anti-inflammatory agents, microbiocenosis restoratives, microcirculation enhancers, and osteotropic drugs on the antioxidant system of the oral cavity in patients with peri-implantitis. By focusing on biochemical markers such as malondialdehyde levels, catalase activity, and the antioxidant-prooxidant index, the study aims to elucidate the potential benefits of augmenting traditional peri-implantitis treatments with antioxidant therapy.

Understanding the role of oxidative stress in peri-implantitis and the efficacy of antioxidant interventions could pave the way for more holistic and effective treatment strategies. Such advancements hold promise not only for improving implant survival rates but also for enhancing overall patient health, given the interconnected nature of oral and systemic conditions [2, 7].

In conclusion, this study aims to contribute to the growing body of knowledge on peri-implantitis by investigating the potential of a therapeutic and preventive complex to enhance antioxidant protection in the oral cavity. The findings may offer valuable insights into the development of more comprehensive treatment approaches that address both microbial and oxidative factors in peri-implantitis management.

The purpose of the study was to evaluate the effect of the treatment and preventive complex on biochemical markers of the antioxidant system in the oral fluid of patients with peri-implantitis.

Materials and methods. Biochemical studies of oral fluid were performed in 40 patients with peri-implantitis aged between 25 and 55 years. Biochemical studies were carried out in the laboratory of biochemistry and vivarium of the SE "The Institute of stomatology and maxilla-facial surgery National academy of medical sciences of Ukraine" (SE "ISMFS NAMS").

Patients were divided into 3 groups:

- 1st group – normal (somatically healthy patients), n=10;
- 2nd group – comparison (patients with peri-implantitis who received basic therapy according to the protocol, n=15);
- 3rd group – main group (patients with peri-implantitis who received a treatment and prevention complex in addition to the basic therapy, n=15).

Patients of groups 2 and 3 had peri-implantitis with a history of concomitant pathology – periodontitis and atherosclerosis.

Patients in the comparison group received basic therapy according to the protocol, while patients in the 3rd (main) group, in addition to basic therapy, received a treatment and prophylactic complex that included drugs with antioxidant, anti-inflammatory effects, agents to restore microbiocenosis and microcirculation, as well as drugs with an osteotropic mechanism of action. The use of this complex was repeated 6 months after the start of treatment.

In the oral fluid of patients, the following were determined: malondialdehyde (MDH) level – an indicator of lipid peroxidation, catalase activity and antioxidant-prooxidant index (API) – an indicator of antioxidant protection of the oral cavity [1].

The results were processed using variational statistical methods of analysis using Microsoft Office Excel 2016 software. Statistical processing of the experimental study results was carried out by the methods of variation analysis using the Student's test. The difference was considered statistically significant at $p < 0.01$ [2].

Results of the study and their discussion. The results of the determination of malondialdehyde in the patients' oral fluid at all stages of the study are presented in Table 1.

From the analysis data, it can be established that at the baseline stage of the study, a significant increase in the inflammatory marker (MDH) was recorded in the comparison group by 1.9 times ($p < 0.001$), and by 1.7 times ($p < 0.001$) in patients of the main group.

After 1 month of basic therapy alone, the level of MDH in the oral fluid of patients with peri-implantitis in the setting of periodontitis and atherosclerosis decreased by only 10.8 % ($p_1 > 0.25$), after 3 months by 16.2 % ($p_1 > 0.6$), after 6 months by 8.10 % ($p_1 > 0.4$), and after 1 year it was 8 % higher than the initial condition ($p_1 > 0.4$).

The additional use of the treatment and prophylactic complex of drugs to the basic therapy in patients of the main group contributed to a significant reduction in the inflammatory marker MDH in the patients' oral fluid during all study periods and corresponded to the indicators of somatically healthy

patients ($p>0.5$). Thus, the study data indicate a high anti-inflammatory and antioxidant efficacy of the developed therapeutic and prophylactic complex of drugs for the treatment of peri-implantitis in the setting of periodontitis and atherosclerosis.

Table 1

Changes in MDA content and catalase activity in patients' oral fluid in the dynamics of treatment, M \pm m

Groups	Terms of the study				
	Initial state	After 1 month	After 3 months	After 6 months	After 1 year
MDA content, mmol/l					
Normal, n=10	0.19 \pm 0.01				
Comparison, n=15	0.37 \pm 0.03 $p<0.001$	0.33 \pm 0.01 $p<0.001$ $p_1>0.25$	0.31 \pm 0.02 $p<0.001$ $p_1>0.6$	0.34 \pm 0.01 $p<0.001$ $p_1>0.4$	0.40 \pm 0.02 $p<0.001$ $p_1>0.4$
Main, n=15	0.32 \pm 0.02 $p<0.001$	0.19 \pm 0.01 $p>0.8$ $p_1<0.001$	0.21 \pm 0.01 $p>0.5$ $p_1<0.001$	0.15 \pm 0.01 $p>0.2$ $p_1<0.001$	0.18 \pm 0.01 $p>0.2$ $p_1<0.001$
Catalase activity, mcg/l					
Normal, n=10	0.30 \pm 0.02				
Comparison, n=15	0.20 \pm 0.02 $p<0.001$	0.22 \pm 0.01 $p<0.001$ $p_1>0.25$	0.16 \pm 0.02 $p<0.001$ $p_1>0.5$	0.17 \pm 0.02 $p<0.001$ $p_1>0.5$	0.19 \pm 0.02 $p<0.001$ $p_1>0.7$
Main, n=15	0.17 \pm 0.01 $p<0.001$	0.24 \pm 0.02 $p<0.001$ $p_1<0.001$	0.27 \pm 0.02 $p<0.05$ $p_1<0.002$	0.29 \pm 0.02 $p>0.7$ $p_1<0.001$	0.32 \pm 0.03 $p>0.5$ $p_1<0.001$

Note. p – significance of differences from the norm; p_1 – significance of differences from the initial level.

The state of the antioxidant system reflects the activity of one of the main enzymes of this system – catalase, which neutralises hydrogen peroxide produced by some pathogenic microorganisms, including *Streptococcus mutans*. Therefore, it is believed that an increase in catalase activity in the oral fluid characterises local resistance to microbial factors.

Before treatment, catalase activity was lower than that of somatically healthy patients in both the comparison group and the main group by 33.3 % ($p<0.001$) and 43.3 % ($p<0.001$), respectively.

Baseline therapy in patients in the comparison group resulted in a slight increase in catalase activity by 10 % ($p_1>0.25$) after 2 months. At more distant periods of the study, catalase activity remained low at 3, 6 and 12 months ($p_1>0.5$, $p_1>0.5$, $p_1>0.7$), respectively. The additional administration of the drug complex to patients in the main group with peri-implantitis against the background of concomitant pathology (periodontitis and atherosclerosis) to the basic therapy contributed to a significant increase in the activity of the antioxidant enzyme at all follow-up periods. Already, 1 month after treatment, this indicator increased by 41.1 % ($p_1<0.001$), a significant increase was recorded in 3, 6, and 12 months by (58.8 %, $p_1<0.001$; 70.5 %, $p_1<0.001$; 88.2 %, $p_1<0.001$), respectively, compared with the pre-treatment values. It should be noted that 1 year after treatment, catalase activity was higher than in somatically healthy patients, indicating a pronounced antioxidant effect of the drug complex.

Thus, along with a decrease in the intensity of lipid peroxidation processes in the oral cavity of patients in the main group, the additional use of a therapeutic and prophylactic complex of drugs contributed to the maintenance of the antioxidant system of the oral cavity, as evidenced by a probable increase in the activity of one of the main enzymes of this system, catalase, in the patients' oral fluid, already 1 month after treatment and throughout the entire observation period.

The state of antioxidant and prooxidant systems is most clearly reflected by the antioxidant-prooxidant index, the results of which are summarised in Table 2.

Table 2

API in the oral fluid of patients at the stages of treatment, M \pm m

Groups	Terms of the study				
	Initial state	After 1 month	After 3 months	After 6 months	After 1 year
Normal, n=10	15.78 \pm 0.65				
Comparison, n=15	5.40 \pm 0.23 $p<0.001$	5.45 \pm 0.31 $p<0.001$ $p_1>0.8$	4.52 \pm 0.21 $p<0.001$ $p_1<0.01$	5.0 \pm 0.29 $p<0.001$ $p_1>0.3$	4.74 \pm 0.21 $p<0.001$ $p_1<0.02$
Main, n=15	5.31 \pm 0.20 $p<0.001$	12.63 \pm 0.65 $p<0.001$ $p_1<0.001$	12.85 \pm 0.67 $p<0.02$ $p_1<0.001$	19.33 \pm 0.78 $p<0.002$ $p_1<0.001$	17.77 \pm 0.84 $p>0.1$ $p_1<0.001$

Note. p – significance of differences from the norm; p_1 – significance of differences from the initial level.

The results of the study showed that peri-implants significantly, more than 2.5 times, reduce the API index at baseline in both study groups of patients. Thus, in the comparison group, during all periods of observation, this index remained at the same level as the initial state, which indicates the suppression of the main link of nonspecific resistance of the oral cavity, as antioxidant protection in peri-implantitis against periodontitis and atherosclerosis.

The use of the therapeutic and prophylactic complex of drugs in patients of the main group in 3 and 6 months relative to the initial treatment period leads to a significant increase in this indicator by 2.3–2.4 times ($p_1 < 0.001$; $p_2 < 0.001$), respectively. The most pronounced changes were observed after 6 and 12 months, this API index exceeded the indicators of the group of somatically healthy patients by 22.4 % ($p < 0.002$) and 12.6 % ($p > 0.1$), respectively, which confirms the presence of antioxidant properties.

This study shows that supplementing basic therapy with a therapeutic and preventive complex significantly enhances antioxidant defenses in patients with peri-implantitis. MDH levels in the oral fluid were markedly reduced to levels comparable with healthy individuals, indicating effective mitigation of lipid peroxidation and oxidative stress. This finding aligns with studies emphasizing oxidative stress as a key factor in peri-implantitis pathogenesis [8, 9]. The significant increase in catalase activity surpassing that of healthy individuals suggests a robust enhancement of the antioxidant defense system. This supports research highlighting the importance of antioxidant enzymes in oral health [7, 12]. The substantial rise in the antioxidant-prooxidant index further confirms the restoration and enhancement of the oral cavity's resistance, especially important for patients with concomitant conditions like periodontitis and atherosclerosis [3, 6]. In contrast, patients receiving only basic therapy did not exhibit significant improvements in MDH levels, catalase activity, or API. This suggests that standard treatments may insufficiently address oxidative stress parameters, highlighting the need for adjunctive therapies. These results support the hypothesis that comprehensive treatment approaches targeting oxidative imbalance can yield better outcomes than therapies focusing solely on microbial reduction [4, 5]. Our findings contribute to the growing evidence supporting the integration of antioxidant therapy in managing peri-implantitis. They underscore the necessity of considering both local and systemic factors in treatment strategies [7]. While oxidative stress has been identified as significant in peri-implantitis, few clinical studies have investigated antioxidant complexes. This study demonstrates the practical benefits of such an approach in improving key biochemical markers associated with the disease.

Conclusions

1. The addition of a therapeutic and prophylactic drug complex to the basic treatment regimen for patients with peri-implantitis significantly reduced malondialdehyde levels, a key marker of lipid peroxidation. This decrease in MDH in the oral fluid aligns with levels observed in somatically healthy patients, demonstrating the drug complex's anti-inflammatory and antioxidant efficacy over extended treatment periods.

2. Catalase activity, a crucial indicator of the antioxidant defense system, was markedly enhanced in patients receiving the drug complex, with a sustained increase up to one year after treatment. This increase was even higher than in healthy individuals, indicating the complex's role in reinforcing local resistance to microbial factors and enhancing overall antioxidant capacity in the oral cavity.

3. The therapeutic and prophylactic complex led to a substantial elevation in the antioxidant-prooxidant index, exceeding the levels found in somatically healthy patients after six months of treatment. This API elevation suggests a restoration and amplification of non-specific oral cavity resistance, emphasizing the complex's potential to sustain long-term antioxidant defense in patients with peri-implantitis amid concomitant conditions like periodontitis.

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CONCURRENT TREATMENT OF CHILDREN'S EPILEPSY AND DEPRESSION

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Epileptic children suffer from depression, and this condition is not well diagnosed and treated, and this results in poor health. The purpose of this work is to evaluate the rate of depression in children with epilepsy and develop an integrated treatment plan. 156 children (aged 12–17 years) with epilepsy were evaluated for depression using Hamilton depression rating scale and the ICD–10 criteria. The current study establishes a high level of depression in children with epilepsy; 68 % of participants fulfilled the criteria for different degrees of depression. Out of the 106 patients diagnosed with depression, 83 had mild depression, 21 moderate and 2 had severe depression. Wilcoxon test showed significant reduction in depression severity after combined anticonvulsant and antidepressant treatment ($p=0.048$). This is especially important in children as the prevalence of epilepsy and depression is high, and both conditions should be treated concurrently. Depression in children with epilepsy should be diagnosed and treated as soon as possible to enhance neurological and psychiatric prognosis.

Key words: epilepsy, depression, children, concurrent disease, treatment.

С.Е. Алієва

ОДНОЧАСНЕ ЛІКУВАННЯ ДИТЯЧОЇ ЕПІЛЕПСІЇ ТА ДЕПРЕСІЇ

Діти з епілепсією страждають від депресії, і цей стан погано діагностується та лікується, що призводить до погіршення здоров'я. Метою даної є оцінка рівня депресії у дітей з епілепсією і розробка комплексного плану лікування. 156 дітей (віком 12–17 років) з епілепсією було оцінено на предмет депресії з використанням шкали оцінки депресії Гамільтона та критеріїв МКХ-10. Поточне дослідження встановлює високий рівень депресії у дітей із епілепсією; 68 % учасників відповідали критеріям для різних ступенів депресії. Зі 106 пацієнтів з діагнозом депресія у 83 була легка депресія, у 21 – помірною та у 2 – тяжкою. Тест Вілкоксона показав значне зниження тяжкості депресії після комбінованого лікування протисудомними та антидепресантами ($p=0,048$). Це особливо важливо для дітей, оскільки поширеність епілепсії та депресії висока, і обидва стани слід лікувати одночасно. Депресію у дітей з епілепсією слід діагностувати та лікувати якомога раніше, щоб покращити неврологічний та психіатричний прогноз.

Ключові слова: епілепсія, депресія, діти, супутні захворювання, лікування.

Epilepsy is a chronic neurological disorder with recurrent unprovoked seizures and is linked with a range of psychiatric disorders, especially depression. Epilepsy in children presents them with a double jeopardy, that of the neurological disease and the other of mood swings. Depression in this group can lead to learning disability, social withdrawal and poor performance in school [1, 3].

The historical data revealed that epilepsy and depression are related conditions. Hippocrates in his writing of 400 BC has noted that “the melancholics are epileptic and the epileptic are melancholic”. Nevertheless, this ancient insight, the comorbidity of epilepsy and depression in children has not received much clinical attention in the present day [2, 8].

Epilepsy epidemiology differs from one country to another all over the world. Epilepsy in Europe and the United States is estimated to be 40–70 cases per 100,000 population. This rate is even higher in developing countries because of factors such as poor health care, and higher incidence of neurological diseases. Research shows that men are more likely to experience epilepsy than women and older men are more vulnerable to epilepsy than young men. Notably, the prevalence of depression in patients with epilepsy differs, with estimates of 22–58 % based on the type, frequency, and compliance with the antiepileptic drugs used [6, 7, 9].