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DYNAMICS OF ORAL FLUID INDICATORS FOLLOWING SIALOSIS TREATMENT IN PATIENTS WITH HYPOTHYROIDISM

Purpose of the study. *To identify changes in oral fluid indicators after the treatment of sialosis in patients with hypothyroidism.* **Research methods.** *Based on the results of a comprehensive examination of 73 patients with hypothyroidism, 7 individuals were found to have the initial stage of sialosis, 57 had the clinically manifested stage, and 9 had the late stage. Mild pain in the areas of the salivary glands was reported by 25 patients, while the remaining patients did not note any discomfort or pain in these areas. Further study was conducted on the 57 patients who had a clinically manifested stage of sialosis on the background of hypothyroidism. These patients were divided into three groups. The first group included 17 individuals who were administered a 1% pilocarpine hydrochloride solution, 4 drops 1–2 times a day. In the second group of 19 individuals, general tonic therapy (AEvit + Vitamin C) was used in combination with physiotherapeutic procedures: ultrasound application of propolis oil in the parotid salivary gland areas. Ultraphonophoresis with propolis oil was performed using an ultrasonic therapy device. The third (control) group consisted of 21 individuals who received general tonic therapy (AEvit + Vitamin C).* **Scientific novelty.** *Our proposed therapeutic and prophylactic regimen – comprising a vitamin complex for general treatment and ultraphonophoresis with propolis oil as a local treatment for sialosis in patients with hypothyroidism – leads to a significant improvement in the condition of the oral cavity. It reduces the size of the salivary glands, decreases inflammation, alleviates dryness of the vermilion border of the lips, eliminates fissures and angular cheilitis, and reduces the size of regional lymph nodes.* **Conclusions.** *Examination of the total protein concentration in the oral fluid of patients with sialosis on the background of hypothyroidism showed elevated levels in all groups at the beginning of the study. Investigation of alkaline phosphatase activity prior to treatment in patients with sialosis and hypothyroidism demonstrated an increased level in all study groups, averaging 0,34 ± 0,017. The data provided indicate that in patients with sialosis associated with hypothyroidism, the oral fluid viscosity remains at a sufficiently high level, which may be a significant factor predisposing to a cariogenic situation and leading to gingival inflammation in the oral cavity.*

Key words: *sialosis, hypothyroidism, salivary glands, oral fluid.*

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ДИНАМІКА ПОКАЗНИКІВ РОТОВОЇ РІДИНИ ПІСЛЯ ЛІКУВАННЯ СІАЛОЗУ В ПАЦІЄНТІВ ІЗ ГІПОТИРЕОЗОМ

Мета дослідження. *Виявити зміни показників ротової рідини після проведеного лікування сіалозу в пацієнтів із гіпотиреозом.* **Методи дослідження.** *На підставі результатів комплексного обстеження 73 пацієнтів із гіпотиреозом у 7 осіб виявили початкову стадію сіалозу, клінічно виражену стадію – у 57 осіб, пізню стадію – у 9 хворих. Незначна болісність у ділянках слинних залоз турбувала 25 пацієнтів, а інші хворі неприємних відчуттів або болю в цій ділянці не відзначали. Подальше дослідження проводили 57 пацієнтам, які мали клінічно виражену стадію сіалозу, на тлі гіпотиреозу. Пацієнтів розділили на 3 групи, до першої групи ввійшли 17 осіб, яким застосовували 1% розчин пілокарпіну гідрохлориду по 4 краплі 1–2 рази на день. У другій групі з 19 осіб використовували загальнозміцнювальну терапію, що включала АЕвіт + Вітамін С і фізіотерапевтичні процедури: ультразвукове введення масла прополісу в ділянках привушних слинних залоз. Ультрафонофорез із маслом прополісу проводили за допомогою апарату ультразвукової терапії. Третя група – група контроля, складалась із 21 особи, використовувалась загальнозміцнювальна терапія, що включала АЕвіт + Вітамін С.* **Наукова новизна.** *Застосування розробленого нами лікувально-профілактичного комплексу, до складу якого входять вітамінний комплекс для загального лікування і ультрафонофорез із маслом прополісу як місцеве лікування сіалозу в пацієнтів із гіпотиреозом, приводить*

до значного покращення стану ротової порожнини, зменшення слинних залоз, зниження запалення в них, усунення сухості червоної облямівки губ, тріщин і заїд у кутах рота та зменшення регіонарних лімфовузлів.
Висновки. *Вивчення концентрації загального білка в ротовій рідині пацієнтів із сіалозом на тлі гіпотиреозу показало його збільшення в усіх групах на початку дослідження. Дослідження активності лужної фосфотази до початку лікування пацієнтів із сіалозом на тлі гіпотиреозу показало підвищений рівень у всіх групах спостереження, 0,34 ± 0,017.*
Наведені нами дані свідчать про те, що в пацієнтів із сіалозом на тлі гіпотиреозу показник в'язкості ротової рідини залишається на досить високому рівні, логічно припустити, що це може бути істотним чинником, що провокує карієсогенну ситуацію та призводить до запалення ясен у порожнині рота.
Ключові слова: *сіалоз, гіпотиреоз, слинні залози, ротова рідина.*

Oral fluid is a unique biological medium. There has been significant interest in examining its indicators for diagnostic purposes since the 1980s. As laboratory methods and equipment have advanced, studying various components of oral fluid has become more accessible [1; 5]. Its physicochemical and biochemical parameters have been characterized, their reference values established for different age groups, and conditions for sample preparation have been defined. It has been determined that oral fluid contains a wide range of proteins and peptides, nucleic acids, as well as electrolytes, enzymes, hormones, and other regulators that originate from both local and systemic sources. This makes oral fluid potentially valuable as a biological medium for assessing not only physiological processes and pathological states in the oral cavity but also throughout the body. In comparison with the traditional method of analyzing blood parameters, determining indicators in oral fluid has several advantages: it is noninvasive, atraumatic to the patient, stress-free, and offers simpler conditions for storage and transportation (due to its liquid state, as opposed to whole blood, which is prone to coagulation). It is also possible to collect the biological material multiple times, facilitating its use in various express laboratories. Despite the interest in the diagnostic value of oral fluid, the main challenge in studying its parameters lies in the insufficient amount of systematized information regarding the role of specific biomolecule assessments for disease detection in clinical practice [3; 6; 7].

Salivary glands (SG) respond sensitively to various changes in the body, reflecting pathological processes occurring within. Clinically, this manifests as a reactive-dystrophic process in the salivary glands against the background of systemic pathology [1; 2]. It is well known that SGs are involved in regulating the digestive activity of the stomach, and numerous authors have noted the development of sialadenosis in patients with carbohydrate metabolism disorders, chronic renal failure, thyroid pathology, reproductive system disorders, and systemic diseases [1; 4; 8].

Viscosity is a measure of the internal friction between adjacent molecules in flowing layers of a fluid. Saliva exists in a micellar state. Proteins that bind large amounts of water contribute to dispersing the entire volume of saliva among micelles, resulting in a structured fluid with high viscosity.

Phosphatases (acid and alkaline) participate in phosphorus-calcium metabolism by cleaving phosphate groups from phosphoric acid compounds and ensuring the mineralization of bones and teeth. Alkaline phosphatase, as an enzyme involved in transporting phosphorus across cell membranes, is an indicator of phosphorus-calcium metabolism. It is present in sufficiently high quantities in the cellular elements of bone tissue, as well as in microorganisms and leukocytes; its levels also increase in oral fluid in the presence of dental pathology.

Alkaline phosphatase requires a pH of 10,0 for its activity. Such a pH value is formed locally upon activation of enzymes that release NH_2 groups in proteins, thereby shifting the pH toward an alkaline environment. Active alkaline phosphatase cleaves phosphate esters of various compounds, releasing phosphoric acid, i.e., phosphorus atoms [1; 7].

Materials and methods of the study. The study included 57 patients who had a clinically manifested stage of sialosis on the background of hypothyroidism. The patients were divided into three groups.

The first group comprised 17 individuals who were administered a 1% pilocarpine hydrochloride solution, 4 drops 1–2 times a day.

The second group (19 individuals) received general tonic therapy (AEvit + Vitamin C) along with physiotherapeutic procedures: ultrasound application of propolis oil in the area of the parotid salivary glands. Ultraphonophoresis with propolis oil was performed using an ultrasonic therapy device.

The third (control) group consisted of 21 individuals who received general tonic therapy (AEvit + Vitamin C).

During the dental examination of all patient groups, general diagnostic principles were employed. The examination of patients with hypothyroidism included a thorough analysis of their complaints, collection of medical history, and an objective examination. In our study, we established a rapport with the patients; by asking guiding questions, we helped

them provide a sequential narrative of their disease history, while analyzing the progression of symptoms. The study was performed in accordance with all deontological rules, considering personal characteristics [7].

Assessment of the condition of the salivary glands and the oral cavity began with identifying complaints and collecting medical history, examined chronologically. We noted the onset of initial symptoms and duration of the disease. Special attention was paid to burning sensations, tingling, or the feeling of a foreign body in the oral cavity, dryness or, conversely, excessive salivation, and its nature. Indirect manifestations of xerostomia were also considered: severe reduction in salivation during emotional stress, inability to eat without drinking water, the need to drink water at night due to severe oral dryness [4].

Most patients with hypothyroidism complained of persistent oral dryness (63,0%), whereas 35% experienced periodic xerostomia during prolonged speaking or emotional stress, as well as during meals. Some patients reported dryness of the oral mucosa arising after enlargement of the salivary glands, and 17 individuals mentioned frequently waking up at night to drink water, with mornings characterized by difficulty separating their lips or opening their mouth [5].

The primary complaint among patients with sialosis on the background of hypothyroidism was painless swelling in the parotid-masseter region, oral dryness, and periodic burning of the tongue, lips, and cheeks, as well as mild pain in the salivary gland areas, reduced hearing acuity, and discomfort in the ears. The aforementioned subjective symptoms were confirmed by objective findings during dental examinations.

It was established that all groups of patients with sialosis and hypothyroidism exhibited hyposalivation, as their initial mean salivation volume across the groups was 0,87 ± 0,04 ml.

All patients were monitored jointly by an endocrinologist and a dentist, allowing for coordinated adjustments in their examination and treatment. A clinical assessment of treatment outcomes was carried out based on patient complaints, overall condition, local signs of disease progression, and data from diagnostic methods.

Saliva collection from individual salivary glands was performed using special cannulae based on the T.B. Andreeva method [1].

After oral administration of 8 drops of a 1% pilocarpine solution and 20 minutes of preliminary bougienage of the ducts, special cannulae were introduced into the ducts of the parotid or submandibular salivary glands. The collection time was 20 minutes after the first drop of secretion appeared. The normal rate of parotid salivary gland secretion is 1–3 ml, while the submandibular glands produce 1–4 ml.

The viscosity of oral fluid was determined using an Ostwald viscometer according to the formula:

$$\Delta_x = \Delta_0 \, t_x/t_0,$$

where Δ_x – viscosity of unstimulated oral fluid;

Δ_0 – relative viscosity of water at a given temperature;

t_x – outflow time of saliva; t_0 – outflow time of water.

Biochemical analyses of oral fluid were conducted before and one month after treatment. Oral fluid was collected in the morning on an empty stomach.

The total protein content in the oral fluid was determined using Lowry's colorimetric method, which is based on the formation of colored products from aromatic amino acids and cysteine upon interaction with Folin's reagent, combined with a biuret reaction to peptide bonds. The protein concentration was expressed in grams per liter (g/L) of oral fluid.

Alkaline phosphatase (AP) activity was determined by the method of O. Bessey (1973), which is based on the hydrolysis of the substrate p-nitrophenyl phosphate, yielding a yellow coloration in an alkaline medium. The intensity of the color corresponds to the enzyme's activity. For measuring AP activity, the substrate was prepared in a glycine buffer with pH 10,5. After hydrolysis, an alkaline medium was created by adding a 0,02% NaOH solution to the incubation mixture. The activity of alkaline phosphatase was expressed in μkat/L (1 katal is the enzyme activity that catalyzes the formation of 1 mole of p-nitrophenol).

Results and Discussion. Our proposed therapeutic and prophylactic regimen – consisting of a vitamin complex for general treatment and ultraphonophoresis with propolis oil for local management of sialosis in patients with hypothyroidism – resulted in a significant improvement in the oral cavity, reduction in the size of the salivary glands, decreased inflammation, elimination of dryness of the vermilion border of the lips, fissures, and angular cheilitis, and a decrease in the size of regional lymph nodes. The presented results demonstrate the positive effect of the proposed treatment and prophylactic complex on salivation volume, viscosity, and the biochemical parameters of oral fluid in patients undergoing sialosis treatment against the background of hypothyroidism.

Changes in the oral fluid viscosity in patients with sialosis and hypothyroidism are presented in Table 1.

Table 1

Dynamics of Changes in Oral Fluid Viscosity in Patients with Sialosis and Hypothyroidism, M ± m

Patient Groups	Before Treatment	After 1 Month
I n = 17	2,57 ± 0,13	1,73 ± 0,09
II n = 19	2,58 ± 0,13	1,61 ± 0,06
Control Group n = 21	2,56 ± 0,13	2,13 ± 0,11

When comparing oral fluid viscosity in patients with sialosis and hypothyroidism across the groups prior to treatment, there were no statistically significant differences ($p > 0,05$). After our treatment, statistically significant differences ($p < 0,05$) were observed in the experimental groups, whereas in the control group there were only minor changes ($p > 0,05$).

Analysis of the results indicates that oral fluid viscosity is elevated in all patients with sialosis on the background of hypothyroidism.

As shown in Table 1, oral fluid viscosity decreased significantly in Groups I and II, but was most pronounced in the group that received additional physiotherapeutic treatment. Thus, these data suggest that in patients with sialosis and hypothyroidism, the viscosity of the oral fluid remains relatively high, likely acting as a significant factor in promoting a cariogenic environment and contributing to gingival inflammation.

An examination of *total protein* concentration in the oral fluid of patients with sialosis and hypothyroidism revealed elevated levels in all groups at the onset of the study (Figure 1), reaching 2,33 ± 0,13 g/L in the first group, 2,29 ± 0,12 g/L in the second, and 2,31 ± 0,12 g/L in the third ($p > 0,05$).

After one month of treatment, the total protein concentration in the first group was 1,32 ± 0,07 g/L, in the second group 1,25 ± 0,09 g/L, and 2,28 ± 0,13 g/L in the third (control) group. Following the use of therapeutic and prophylactic agents, numerical values for total protein concentration in the oral fluid of sialosis patients with hypothyroidism were lower in the first two groups, whereas the control group did not show a statistically significant decrease ($p < 0,05$) (Figure 1).

Study of *alkaline phosphatase activity* prior to treatment in patients with sialosis and hypothyroidism showed elevated levels in all observation groups (0,34 ± 0,017, 0,35 ± 0,013, 0,34 ± 0,018 μkat/L), obviously due to abnormalities in both dental conditions and thyroid gland pathology.

One month after treatment, AP activity values tended to decline. In the first group (pilocarpine solution), the indicator was 0,28 ± 0,014 μkat/L; in the second group (physiotherapeutic methods), 0,26 ± 0,013 μkat/L; and in the third group, 0,31 ± 0,017 μkat/L, indicating only a minor change (Figure 2).

Statistically significant differences in AP activity were found in the first and second groups ($p < 0,05$). In the third group, the decrease in the indicator was minor ($p > 0,05$).

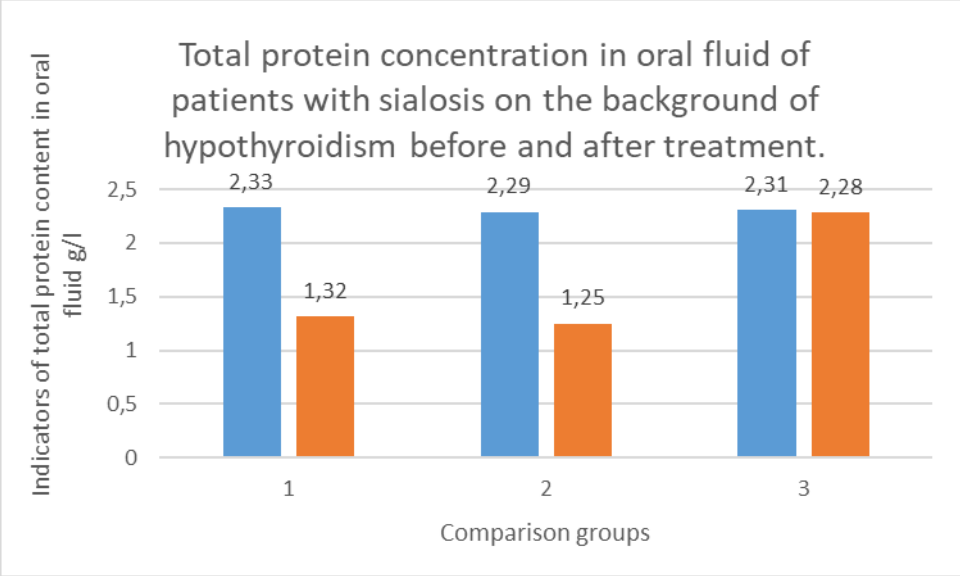

Fig. 1. Total protein concentration in the oral fluid of patients with sialosis and hypothyroidism

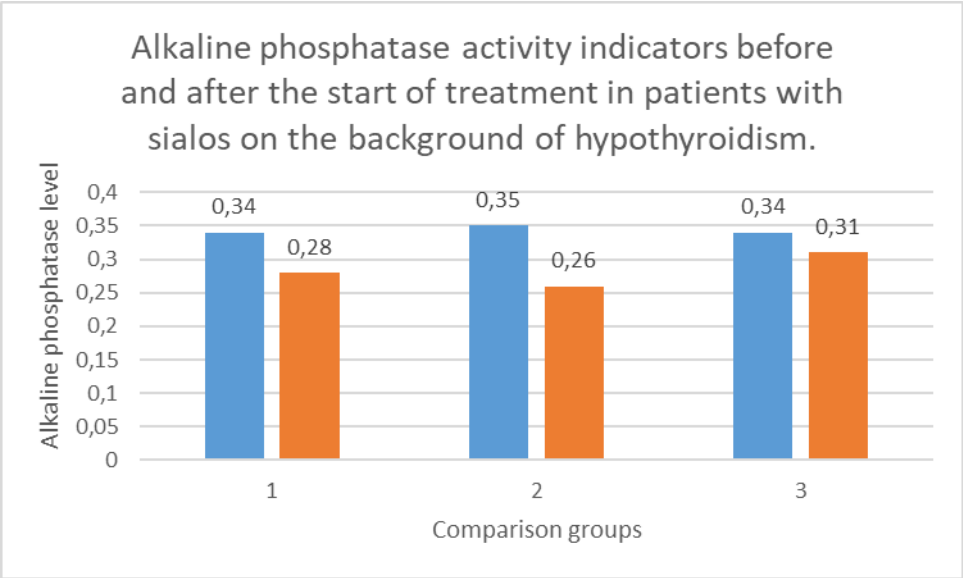

Fig. 2. Alkaline phosphatase activity before and after treatment in patients with sialosis and hypothyroidism

Conclusions:

1. Examination of total protein concentration in the oral fluid of patients with sialosis and hypothyroidism revealed elevated levels in all groups at the onset of the study, averaging 2,31 ± 0,12 g/L.

2. Investigation of *alkaline phosphatase activity* prior to treating patients with sialosis on the background of hypothyroidism showed elevated levels across all observation groups, with a mean of 0,34 ± 0,017 μkat/L.

3. The use of our proposed therapeutic and prophylactic regimen – including a vitamin complex for general treatment and ultraphonophoresis with propolis oil as local therapy for sialosis in patients with hypothyroidism – led to a significant improvement in the oral cavity, reduction in salivary gland size, decrease in inflammation, elimination of dryness of the vermilion border of the lips, fissures, and angular cheilitis, and a decrease in regional lymph nodes.

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