REPUBLIC OF AZERBAIJAN

On the rights of the manuscript

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

ASSESSMENT OF DENTAL STATUS AND WAYS OF ITS CORRECTION IN PATIENTS WITH HYPOTHYROIDISM

Specialization: 3226.01 – Dentistry

Field of science: Medicine

Applicant: **Latafat Aydin Aliyeva**

Baku – 2024

The work was performed at the Department of Oral and Maxillofacial surgery of Azerbaijan Medical University.

Scientific supervisor: doctor of medical sciences, professor
Tamara Hajibaba Huseynova

Official opponents: doctor of medical sciences, professor
Zohrab İslam Qarayev

doctor of medical sciences, professor
Afet Rashid Agazade

doctor of medical sciences
Kamal Qafar Qafarov

Dissertation Council ED 2.50 of the Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the Azerbaijan Medical University.

Chairman of the Dissertation Council:
doctor of medical sciences, professor
Vafa Mustafa Panahian

Scientific Secretary of the Dissertation Council:
doctor of medical sciences, professor
Aga Chingiz Pashayev

Chairman of the Scientific Seminar:
doctor of medical sciences, professor
Rana Gurban Aliyeva

İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb elmləri doktoru, professor
Nazim Adil oğlu Pənahov
08.04.24

GENERAL CHARACTERISTICS OF THE RESEARCH WORK

Relevance of the topic and degree of the research. Thyroid disorders are a common pathology and remain a clinical problem[1]. Thyroid disease holds a dominant position among endocrine disorders. According to the WHO, more than 200 million people in the world suffer from thyroid dysfunction[2].

The annual incidence of primary hypothyroidism is 3.5 per 1000 women and 0.6 per 1000 men. The incidence of hypothyroidism increases significantly with age[3].

Both internal and external environmental factors affect the dental condition of the body. The participation of thyroid hormones in many metabolic processes, as well as the maintenance of calcium and phosphorus homeostasis signifies the effect of the thyroid gland on the state of overall dental health[4]. Also, the high prevalence of dental pathologies is contributed to the decrease in the content of vitamins in the body, found in hypothyroid patients[5].

With thyroid dysfunction, there are violations of the formation and eruption of temporary and permanent teeth, increased rate of carious damage, inflammatory and degenerative processes in the periodontium and gums, ulcerations, destruction of the alveolar processes of

---

[1] Chaker, L. Hypothyroidism / L. Chaker, S. Razvi, I.M. Bensenor [et al.] // Nature Reviews Disease Primers, – 2022. 8 (30), – p. 1-17.

[2] Keestra, S., Tabor, V.H., Alvergne, A. Reinterpreting patterns of variation in human thyroid function An evolutionary ecology perspective // Evolution, Medicine, and Public Health, – 2021. – p. 93-112.

[3] Бирюкова, Е.В., Килейников, Е.В., Соловьева, И.В. Гипотиреоз: современное состояние проблемы // - Москва: Медицинский совет, – 2020. №7, – с. 96-107.

[4] Артеменко, Т.В., Сахарук, Н.А. Анализ стоматологического здоровья у пациентов с эндокринной патологией (гипотиреоз) // - Витебск: Вестник витебского государственного медицинского университета, –2014. № 2, – с. 124–128.

[5] Дьяченко, С.В. Влияние гипофункции щитовидной железы на стоматологическое здоровье лиц пожилого возраста / С.В. Дьяченко, И.В. Фирсова, А.Т. Яковлев [и др.] // - Владивосток: Тихоокеанский медицинский журнал, – 2020. №1, – с. 14-8.

mandible and maxilla[6]. People suffering from thyroid dysfunction have aggressive oral diseases such as bone loss, root resorption and layering of dental tissues due to periodontal disease. Consequently, this population becomes more vulnerable and at higher risk of developing oral infections. Regular two-way communication between oral health specialists and endocrinologists is an important component of the treatment of patients suffering from thyroid dysfunction[7].

Given the great potential of derivatives based on hyaluronic acid, a large number of clinical studies has been devoted to the study of the effectiveness of the use of these substances in periodontology[8].

The level of vitamin D in the blood serum plays an important role in the formation of homeostasis of the oral cavity. Deficiency of this vitamin affects the health of the maxillofacial area, which is important in clinical, physiological, psychological and social aspects[9]. The involvement of vitamin D in the pathogenesis of periodontitis is biologically plausible.

Clinical studies have consistently demonstrated an inverse relationship between serum 25OHD3 and inflammation in periodontal disease[10].

The nature of changes in bone structure in persons with hypothyroidism and vitamin D deficiency indicates the need for thyreostatic

---

[6] Городецкая, И.В., Масюк, Н.Ю. Влияние йодсодержащих тиреоидных гормонов на ткани челюстно-лицевой области // - Витебск: Вестник Витебского государственного медицинского университета, – 2018. №2, – с. 20-25.

[7] Сигаева, Н.Н. Химическая модификация гиалуроновой кислоты и ее применение в медицине / Н.Н. Сигаева, С.В. Колесов, П.В. Назаров [и др.] // - Уфа: Вестник Башкирск. ун-та, - 2012. №3, - с. 1220-1241.

[8] Тарасенко, С.В., Кулага, О.И. Препараты на основе гиалуроновой кислоты для лечения пациентов с хроническим генерализованным пародонтитом // - Москва: Российский стоматологический журнал, – 2016. №6, – с. 340-343.

[9] Ноговицина, А.А. Влияние D-витаминной недостаточности в организме на состояние полости рта молодых людей / А.А. Ноговицина, Е.П. Лашманова, С.Н. Саблина [и др.] // Международная (75 Всероссийская) научно-практическая конференция «Актуальные вопросы современной медицинской науки и здравоохранения». – Москва, – 2020, – с. 247-252

[10] Agrawal, A.A. Evaluation and Comparison of Serum Vitamin D and Calcium Levels in Periodontally Healthy, Chronic Gingivitis and Chronic Periodontitis in Patients with and without Diabetes Mellitus–a Cross –Sectional Study / A.A. Agrawal,

therapy with the administration of vitamin D [11].

In this regard, researching dental manifestations of hypothyroidism and finding ways to correct them is of particular relevance today.

The object and subject of the study. A comprehensive examination of 300 people was carried out, including 150 people suffering from thyroid hypofunction and 150 somatically healthy individuals from 19 to 45 years old. Patients were divided into three age groups: 19-29 years old, 30-39 and 40-45 years old. The subject of the study was to identify the characteristics of periodontal health in patients with hypothyroidism, as well as to establish the effectiveness of complex treatment and its impact on the further development of chronic generalized periodontitis.

The aim of the study was increase the effectiveness of periodontitis treatment in patients with hypothyroidism by etiopathogenetic correction of local immune and dysbiotic disruptions.

The study objectives:

1. To study the frequency of occurrence and features of clinical manifestations of major dental pathologies in patients along with hypothyroidism.

2. To establish the features of clinical indicators of periodontal disease in patients with hypothyroidism and to identify the frequency and nature of lesions of the salivary glands in patients with hypothyroidism and study the degree of their influence on the secretory activity of the salivary glands.

3. To study salivation and immunological changes in the oral cavity in patients with chronic generalized periodontitis concurrent with hypothyroidism.

4. To study the effect of complex treatment with and without the use of a combination of calcium + vitamin D on the clinical course of chronic generalized periodontitis concurrent with hypothyroidism.

5. To study biochemical and microbiological changes in the oral cavity in patients with hypothyroidism with the use of hyaluronic acid and substantiate the expediency of its use.

---

[11] Вахрушева, В.Ч. Связь между патологией щитовидной железы и заболеваниями пародонта / В.Ч. Вахрушева, П.И. Астрюхина, Д.О. Кокшарова [и др.] // - Москва: StudNet, – 2022. № 3, – с. 1696-1714.

Research methods. The research methods included the following parameters:

- measurement of salivation rate, pH measurement of saliva
- clinical index scoring
- microbiological and biochemical examination of saliva
- statistical processing of the obtained data.

The main provisions for the defense:

- The high prevalence of inflammatory periodontal diseases and adverse reactions of some potent drugs predetermine the timeliness of using optimal complex therapeutic and preventive measures.

- Therapeutic methods and measures based on vitamin D and hyaluronic acid applications can be used in periodontal treatment and rehabilitation of patients with endocrine deficiencies in all age and sex groups.

Scientific novelty of the study:

- Proposals have been developed for organizing and conducting a biannual dental observation for patients with hypothyroidism and vitamin D deficiency under the supervision of an endocrinologist.

- As a result of clinical and laboratory studies, clinical and laboratory parameters were determined and new data was obtained on the state of the oral cavity before and after the use of a combination of calcium + vitamin D in complex periodontal treatment in patients with hypothyroidism.

- The importance of including a combination of calcium + vitamin D in the complex of therapeutic and preventive measures to reduce the frequency of relapses in patients with hypothyroidism and vitamin D deficiency has been revealed.

- On the basis of clinical and laboratory data, the preventive and therapeutic effect of hyaluronic acid in the treatment of mild to moderate gingivitis and periodontitis has been scientifically substantiated and practically demonstrated.

The practical significance of the study:

- Patients with hypothyroidism and vitamin D deficiency in the body should be included in the risk group for the development of early, steadily rapidly progressing and severe forms of inflammatory and destructive changes in their dental health.

- Informative data obtained from a comparative analysis of clinical and laboratory parameters and the most significant information identified will contribute to an accurate and timely assessment of the degree of damage to organs and tissues of the oral cavity occurring with hypothyroidism and vitamin D deficiency.

- Based on the results of clinical and laboratory analysis, an effective method of treating gingivitis, mild and moderate periodontitis in patients with hypothyroidism and vitamin D deficiency was developed and proposed.

- The data obtained is promising and can be used for accurate and timely diagnosis, identification of pathological disorders in the organs and tissues of the oral cavity and will allow us to recommend hyaluronic acid, as well as vitamin D therapy in patients with hypothyroidism.

- The developed methods in the course of scientific research, upon receipt of positive data results, can be applied in dental clinics and hospitals. This will create the opportunities to recommend the use of biologically active medicines, vitamin therapy (vitamin D) and improve the results of complex treatment of mild, moderate gingivitis and periodontitis, reduce the number of complications and relapses, and improve the quality of life of patients with hypothyroidism.

Approbation. The main points of the thesis report and discussion was carried out at conferences: "Science and innovation" modern concepts, Moscow, 2020; The 5th International Scientific Congress on "Modern Problems in Pharmaceuticals" dedicated to the 90th anniversary of the establishment of Azerbaijan Medical University and the 80th anniversary of HIGH Pharmaceutical Education in Azerbaijan, Baku, 2021; XXII international scientific and practical conference " Current problems in dentistry", dedicated to the 25th anniversary of the Azerbaijan Dental Association. Baku, April 1-3, 2023

Dissertation materials were discussed at the extended meeting of the Department of Oral and Maxillofacial Surgery with the participation of employees of other specialized dental departments of Azerbaijan Medical University (June 23, 2022, protocol No. 10), a

scientific seminar operating under the Dissertation Council ED 2.05 (October 31, 2022, protocol No. 17).

Implementation of research results into practice. Scientific and educational-practical data obtained as a result of these studies will be introduced into the practice of the AMU Dental Clinic, as well as into the educational process of the specialized dental departments.

The name of the organization where the dissertation work was performed. The research work was carried out at the Department of Oral and Maxillofacial Surgery of the Azerbaijan Medical University and at the Republican Endocrinological Center.

Publication. 10 scientific work were published on the topic of the dissertation, including 2 articles and 1 thesis abroad.

The volume and structure of the dissertation. The dissertation work is written on 171 pages (200.800 symbols) in the Russian language. The dissertation consists of an introduction (15.500 symbols), a literature review (62.200 symbols), a chapter on materials and methods of research (37.800 symbols), chapter covering own research (50.300 symbols) conclusions, results, practical recommendations (35.500 symbols) and a list of scientific literature containing 189 sources, both domestic and and foreign scientists. The dissertation includes 25 tables and 18 graphs.

MATERIALS AND RESEARCH METHODS

The dissertation research was carried out in accordance with the principles and rules of evidence-based medicine. A comprehensive examination of 300 people with various forms of periodontopathies was carried out, including 150 patients suffering from thyroid hypofunction aged 19 to 45 years) and 150 somatically healthy individuals.

Treatment for all patients included oral hygiene instructions. Patients with a mild degree of periodontal pathologies underwent closed curettage aimed to relieve inflammatory processes, open curettage was recommended for moderate severity, and flap surgeries

were planned for severe cases.

The level of prevalence and need for periodontal care were assessed using WHO recommendations applying Community Periodontal Index of Treatment Needs - CPITN, 1980.

The frequency and intensity of caries was determined by the DMFT index, which took into account the number of decayed (D), missing (M), filled (F) Teeth (T). To examine the condition of the periodontium, periodontal and hygienic indices were used: plaque index Silness - Loe (Silness - Loe, 1964), Sulcular Bleeding Index (SBI, Muhlemann, Cowell, 1971), effectiveness of oral hygiene using Patient Hygiene Performance index (PHP, Poshadley A.G., Haley P., 1968) and Bleeding on Probing index (BOP, Ainamo, Bay, 1975), Periodontal Indeks (PI Russel, 1956) and other. Biochemical research obtained data for SOD, catalase, MDA and immunoglobulins in saliva. Microbiological studies obtained data for presence of major periopathogens. While examining patients, the presence of carious and non-carious dental lesions, bleeding on probing, purulent exudate, the presence and depth of periodontal pockets, the degree of tooth mobility and dental plaque were assessed. In accordance with the purpose and objectives, the selection of patients took into account patients' age, gender, place of residence, profession, duration of the course and severity of underlying somatic condition.

All study participants were divided according to age into 3 age group categories– from 19 to 29 years old, from 30 to 39, from 40 to 45. Patients with hypothyroidism were further divided into two large treatment groups. The first treatment group, consisting of 36 people, was further divided into 3 subgroups: the main, control and comparison group. Local treatment in the control group – 12 people, included the removal of dental plaque, closed curettage as part of individual oral hygiene. In the second group, the comparison group – 11, a traditional antiseptic was used, all patients underwent removal of tartar with an ultrasonic scaler and irrigation of the gums with 0.05% chlorhexidine solution. In the third main group – 13, the complex of therapeutic measures additionally included applications of hyaluronic acid for 20 minutes daily for 14 days ("Hyalgan").

In the second treatment group, 31 patients with mild chronic generalized periodontitis aggravated by vitamin D deficiency in the body with underlying hypothyroidism were selected from the total number of patients.

Then using a simple random sampling method, patients of the second treatment group with thyroid hypofunction and vitamin D deficiency who participated in the study were divided into clinical groups depending on the prescribed course of treatment:

- Group I – 15 patients with mild chronic generalized periodontitis with a level of 25(OH)D< 50 nmol/l in blood serum, who underwent traditional complex treatment of periodontitis without medical correction of vitamin D levels.

- Group II – 16 patients with mild chronic generalized periodontitis with a level of 25(OH)D< 50 nmol / l in blood serum, who underwent traditional treatment of periodontitis with simultaneous correction of vitamin D level (vitamin D3 + calcium).

Statistical analysis of the results was performed using the IBM Statistics SPSS-26 program (USA). To compare the results between groups, Pearsons' $\chi 2$ criteria and Students' t-test, Students' d-test and nonparametric methods – Mann-Whitney U-test and Wilcoxon T-test were used.

RESEARCH RESULTS AND THEIR DISCUSSION

Analysis of the CPITN index value showed that among patients with hypothyroidism, the incidence of periodontal diseases was approximately 96% of cases. The frequency of gum bleeding was minimal and was determined to be 6.00±1.94%. The highest values in patients of all three age groups were recorded in relation to dental calculus. Dental calculus deposits were detected in 44.7±4.06% of the examined patients. Periodontal pockets were more often detected in groups of older patients and were diagnosed in 28.0±3.67% and 17.3±3.09% of cases. Periodontal pockets with a depth of up to 4-5 mm predominated. After analysis of the index data, the severity of the formation of hard dental plaque was

2.34±0.10 sextant. Thus, in the first group, 26.0±6.20% and 14.0±4.91% of the examined patients with hypothyroidism had periodontal pockets 4-5 mm, with an intensity of 1.26±0.14 sextant, 6 mm and > at an intensity of 0.66±0.11 sextants, respectively (Table 1).

Table 1
Community Periodontal Index of Treatment Needs in patients with hypothyroidism (CPITN)

Age groups	Examined	Average number of sextants				
		Healthy Periodontium	Bleeding	Dental calculus	Periodontal Pockets	
					4-5 mm	6 mm and more
19-30 years	50	0.92±0.13	0.90±0.13	2.04±0.17	1.26±0.14	0.66±0.11
30-39 years	60	0.15±0.05	0.32±0.07	2.38±0.16	1.98±0.15	0.85±0.11
40-45 years	40	-	0.20±0.07	2.65±0.21	1.68±0.19	0.68±0.13
Total	150	0.37±0.05	0.48±0.06	2.34±0.10	1.66±0.09	0.74±0.07

The largest number of sextans with dental calculus was detected in the age group of 40-45 years, where it was 2.65±0.21. It is evident that the presence of background endocrinological pathology together with poor oral hygiene is reflected in the condition of the soft and hard periodontal tissues.

The identified tendency towards an increase in the frequency and intensification of periodontal diseases, especially its severe forms, is associated with poor oral hygiene and the presence of concomitant background endocrine pathology.

In patients with hypothyroidism, the periodontal index (PI) value was 1.6 times higher than in practically healthy individuals. In patients with hypothyroidism, the gingival index was higher than in the control group: 0.97±0.016 points and 0.54±0.009 points, respectively ($p < 0.001$). Consequently, in patients with underlying pathology, the course of the inflammatory process is more intense

and develops within a short time to severe degrees of periodontopathies. When assessing the dental status and condition of the periodontal tissues in patients with hypothyroidism, mild periodontitis was detected in 16.7% cases. Whereas mild forms of the inflammatory process in periodontal tissues were significantly more often observed in the control group of persons without background pathology - 63.3% ($\chi 2 = 69.06$; $p < 0.001$).

When studying the periodontal status of those examined with reduced thyroid function, chronic generalized moderate periodontitis was diagnosed in 55.3% of cases. Comparative analysis between groups of patients with and without hypothyroidism showed that mild degree periodontitis was 73.6% less common in patients with thyroid hypofunction. Moderate and severe forms of periodontal disease, respectively, 50.6% and 66.8% were more prevalent in hypothyroid patients than in healthy patients. In patients with hypothyroidism, the gingival index was much higher than in the control group: 0.97±0.016 points and 0.54±0.009 points, respectively ($p<0.001$). A severe degree of periodontal pathology of the inflammatory-destructive nature was found in 28.0% of cases of patients with hypothyroidism versus 9.3% in the control group.

In persons suffering from hypothyroidism for just one year, mild generalized periodontitis was detected in 36.0% of cases, moderate - in 54.0%, and the most severe periodontal pathologies were diagnosed in 10.0% of patients. In patients suffering from endocrine pathology for a longer period (1-4 years) periodontitis of moderate severity was most often detected, the frequency of its occurrence in this time interval was 66.7%. While in patients aggravated by hypofunction of the thyroid gland for 5 or more years, the indicators for this factor were fixed at 40.0% ($\chi 2=43.16$; $p<0.001$). In persons suffering from hypothyroidism for 5 or more years, when analyzing the condition of periodontal tissues and the degree of the inflammatory process, severe chronic generalized periodontitis was observed much more often, in comparison to other forms of dental pathology - in 60.0% of the examined patients.

In general, mild periodontitis was more often detected in patients in whom the duration of somatic pathology did not exceed 1

year. The moderate form of periodontitis prevailed in patients with hypothyroidism lasting 1-4 years, and more severe inflammatory and destructive processes in the periodontium were recorded with a longer course of endocrine disease.

In 3 clinical groups of patients with hypothyroidism, quantitative indicators that indicated the need for hygiene training and, consequently, the need to improve hygiene, amounted to 6.0±1.94% on average. Among the patients, the need for professional hygiene with the removal of dental calculus and the elimination of factors that promote growth of dental plaque was generally present in 90.0±2.45% of patients.

The pH level of unstimulated mixed saliva in all subjects was low; two weeks later in the male and female groups in patients with hypothyroidism there was a sharp increase in pH: from 7.10 ± 0.07 rel. units up to 7.52±0.05 rel. units ($p_1<0.001$) and in the first group with 7.06±0.03 rel. units up to 7.43±0.02 rel. units ($p_1<0.001$). After 3 months, in groups 1 and 2, the pH value of the oral fluid decreased slightly, but remained shifted to the alkaline side.

Studies have shown a high increase in the examined patients with hypothyroidism of E. Coli from conditionally pathogenic microorganisms of the Enterobacteriaceae family, which amounted to 4.99±0.14x105 CFU/ml, versus 4.95±0.10x104 CFU/ml in those examined without thyroid disorder. Accelerated growth of yeast-like fungi of the genus Candida albicans was often detected ($4.87±0.07x10^4$-10^8 CFU/ml) in the main group.

The study of the oral fluid in patients before the start of treatment showed that in the oral cavity with the development of an inflammatory process in periodontal tissues along with somatic pathology, MDA accumulates with a sharp decrease in the quantitative indicators of the activity of antioxidant defense enzymes – a decrease in the amount of SOD and catalase, which, in turn, testified to a pronounced intensification of the process of free radical lipid oxidation (Table 2).

Table 2
Biochemical parameters of saliva in patients before and after treatment

Groups	Terms	Indicators		
		MDA, nmol/ml	SOD, %	Catalase activity, mkat/l
Main group Group 1, n=13	Before treatment	1.08±0.05	42.4±0.26	43.1±0.29
	After treatment	0.71±0.03	45.3±0.18	46.2±0.20
	P	<0.001	<0.001	<0.001
Control group Group 2, n=12	Before treatment	1.97±0.05	34.6±0.68	36.1±0.45
	After treatment	1.30±0.03	37.2±0.36	38.7±0.64
	P	<0.001	0.004	0.004
Comparison group Group 3, n=11	Before treatment	4.04±0.24	23.5±0.31	22.3±0.44
	After treatment	2.89±0.15	40.2±0.45	34.5±0.38
	P	<0.001	<0.001	<0.001

Note: P is the statistical value of the difference relative to before treatment (T-Wilcoxon test)

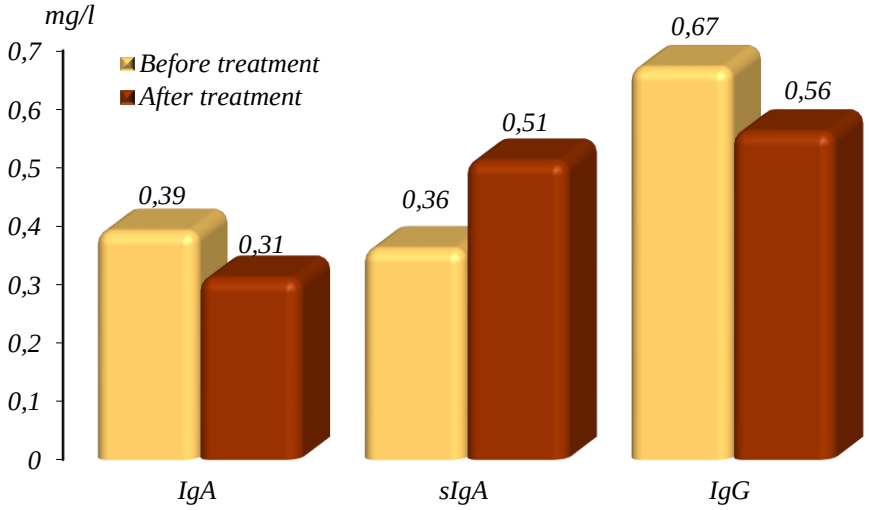
The most favorable situation is observed in patients with mild gingivitis and periodontitis in the main group, where the level of peroxidation was the lowest in comparison with the control group and the comparison group. Thus, the level of MDA after completing the course of basic therapy in groups was equal to 0.71±0.03 nmol/ml, 1.30±0.03 nmol/ml and 2.89±0.15 nmol/ml, respectively, in the main, control group and in the comparison group. In addition, these same patients before treatment had a high level of lipid peroxidation products and a reduced level of antioxidant defense enzymes in the oral cavity (p <0,05). This situation was observed in patients of all three groups, but the dynamics of indicators identified by some important factors was of a more pronounced anti-inflammatory nature and was obtained on the 14^{th} day after exposure to hyaluronic acid in periodontal pockets.

In patients of the examined groups, data was obtained on the differences in quantitative indicators of catalase before and after therapeutic measures. Thus, the results of treatment of periodontitis indicated a significant increase in the level of catalase in the oral fluid

during the use of traditional therapy from 22.3±0.44 mkat/l to 34.5±0.38 mkat/l (p<0,001) in comparison group patients. The patients of the other two therapeutic groups were no exception.

Thus, we can state the fact of the positive influence of hyaluronic acid on the normalization of the balance between free radicals and antioxidant systems and on the increased stability of periodontal tissues, as evidenced by a slight decrease in the content of MDA in mixed saliva and an increase in the quantitative indicators of SOD.

Biochemical studies of saliva and the content of immunoglobulins in it in patients of all three groups with somatic pathology revealed a significant decrease in the amount of sIgA and a moderate increase in IgG in a similar environment, which indicated a weakening of their local humoral immunity (Graph 1).



Graph 1. Immunoglobulin content in saliva before and after the use of hyaluronic acid (I group, n=13)

The use of hyaluronic acid as a means of anti-inflammatory and supportive therapy contributed to a sharp increase in sIgA and correction of the IgG content in saliva, and, to a certain extent, restoration of

the barrier function of organs and tissues of the oral cavity.

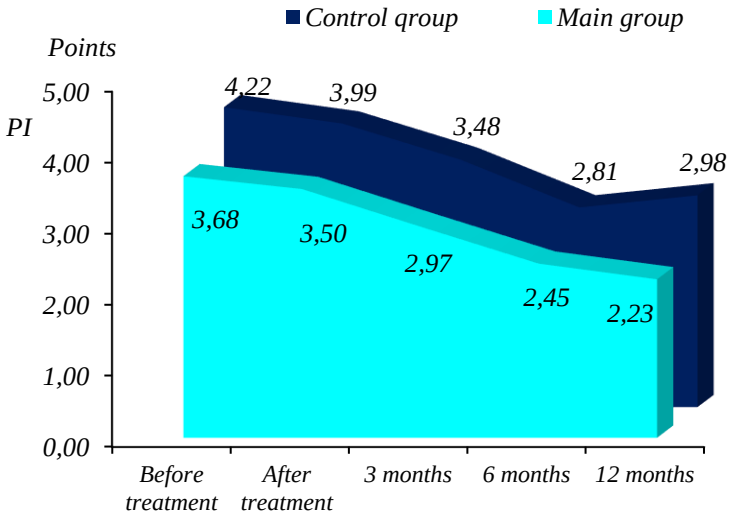
The level of sIgA after professional oral hygiene and the traditional antiseptic 0.05% chlorhexidine bigluconate increased in comparison group from 0.34±0.019 mg/l to 0.42±0.022 mg/l (p=0.009).

The weakening of the inflammatory process after the therapy was evidenced by a decrease in the content of class G immunoglobulin in the oral fluid - from 0.68±0.030 mg/l to 0.54±0.021 mg/l, respectively, before and after the completion of applications of the traditional antiseptic (p=0.002).

According to the data obtained, the risk factors for the onset and development of inflammatory periodontal diseases in the examined patients in the control group include very low quantitative indicators of sIgA and a sharp increase in the level of IgA and IgG immunoglobulins in the oral fluid.

Timely implementation of rehabilitation measures such as removal of dental plaque, treating carious lesions, removal of the roots of decayed teeth and the appointment of effective hygiene products in the course of complex treatment ensures a relative normalization of local immunity and regression of clinical symptoms of inflammation. The results of biochemical studies in control group showed a more pronounced trend in the normalization of the content of immunoglobulins sIgA in comparison with other groups of patients – 0.46±0.023 mg/l in the control group.

The statistical data shows that in patients who took vitamin D supplementation for a certain period of time, not only serum indicators of vitamin D changed, but also the condition of soft and hard periodontal tissues significantly improved. The Russell index changed significantly in the main group and least of all in the control group. In patients with somatic pathology in the main group it decreased from 3.68±0.023 points to 3.50±0.020 points ($p<0.05$) immediately after treatment (Graph 2).



Graph 2. Change in the periodontal index (PI) in patients with hypothyroidism in dynamics, points.

A similar picture in the same period or stage is also observed when analyzing the index values in the control group. With approximately similar dynamics of improvement in the condition of the periodontal tissues with conjunction of ongoing therapy, a more pronounced prolonged therapeutic effect can be seen when vitamin D is included in the basic therapy.

In the main group, when analyzing the long-term results, the value of the periodontal index at the final stage of clinical observations was 2.23±0.032 points, with a value of 2.98±0.020 points found in the control group ($p<0.05$). The indicators for other indices were significantly better compared to the previous data in patients of the main group. At the same time, the long-term effect after completion of treatment indicated the stability of the results obtained.

The inclusion of vitamin and mineral combination in the complex etiopathogenetic treatment of mild chronic generalized periodontitis in

patients with hypothyroidism and vitamin D deficiency leads to positive dynamics of clinical indicators, for example, PMA index and GI index improved compared to initial data in main group. At the same time normalization is detected in the redox potential and the pH level of the oral fluids ($p<0.001$). When studying the dynamics of increase / decrease in periodontal pocket bleeding during probing with a Williams button probe and determining the BOP index, it was found that in the main group there was a decrease in gingival bleeding in both groups of examined somatic and dental patients already at the initial stage of the study, but more pronounced and significant changes in improvement in performance was recorded in the main group.

Immediately after the completion of therapeutic and preventive measures in the main group, gum bleeding during probing decreased from 80.2±1.09% to 20.8±0.94% ($p<0.001$), respectively, in relation to the data obtained before the start of the study (values statistically significant).

Indicators of the papillary-marginal alveolar index decreased in all groups of the study, but in the long-term results, a more pronounced positive trend was observed only in patients in the main group. So, for example, if the values of the studied index by the end of observations, that is, 1 year after the completion of periodontal treatment, in the control group amounted to 26.8±0.57%, then in the same time period the indicators of the periodontal index in the main group decreased to the minimum level – 15.2±0.67% ($p<0.05$).

One of the main destabilizers of the acid-base balance in mixed saliva is dental plaque. Metabolic processes under anaerobic conditions are an etiopathogenetic factor in the occurrence and development of pathology of hard dental tissues or inflammatory periodontal diseases. Normally, that is, in an intact state, the pH of saliva in an adult varies between 6.9-7.3, and in children on average it reaches a value of 7.3-7.35. The pH value of the oral fluid after treatment increased in all groups, especially in the main group (Table 3).

Table 3
Salivation Rate and pH change dynamics

Terms of observation	Salivation rate, mg/min pH		pH	
	Control group, n=15	Main group, n=16	Control group, n=15	Main group, n=16
Before treatment	0.60±0.014	0.59±0.015	6.83±0.081	6.84±0.076
After treatment	0.83±0.007 p<0.001	0.61±0.008 p>0.05 p_1<0.001	6.72±0.009 p>0.05	6.91±0.030 p>0.05 p_1<0.001
After 3 months	0.87±0.021 p<0.001	0.68±0.010 p<0.01 p_1<0.001	6.74±0.010 p>0.05	6.94±0.027 p>0.05 p_1<0.001
After 6 months	0.61±0.020 p>0.05	0.64±0.013 p<0.05 p_1>0.05	6.80±0.011 p>0.05	6.99±0.020 p>0.05 p_1<0.001
After 12 months	0.57±0.009 p>0.05	0.67±0.015 p<0.001 p_1<0.001	6.84±0.023 p>0.05	7.03±0.029 p<0.05 p_1<0.001

Note: the reliability of the results in relation:
p - to the data before treatment;
p1- to the data of the control group

In the main group, 24 weeks after treatment, where a vitamin-mineral complex was prescribed in the treatment regimen, a pH value of 6.94±0.027 was recorded, versus pH=6.74±0.010 in the control group (p1<0.001). In subsequent observation periods, there was also a significant increase in the acid level indicator in comparison with the control group. This is indicated by the pH level in saliva after 6 and 12 months – 6.99±0.020 (control - 6.80±0.011, p1<0.001) and 7.03±0.029 (control - 6.84±0.023, p1<0.001) respectively. The rate of salivation in patients of the main group immediately after treatment was practically no different from the initial one (p>0.05), while in the control group it increased from 0.60±0.014 to 0.83±0.007 (p<0.001). However, at later examinations, after 6 and, especially, 12 months, the rate of salivation in those examined in the main group was higher than

the initial ($p<0.05$) and control indicator ($p1<0.001$).

In the control group, pH also increased at all subsequent stages of the study in comparison with the initial value; these decreases were less pronounced and not significant compared to the main group ($p>0.05$). This confirms the low effectiveness of the traditional method of treatment, compared to our proposed individual complex method for the prevention and treatment of periodontal diseases in patients with hypothyroidism and a deficiency of vitamin D. Laboratory observation of patients showed that the inclusion of pharmacological correction of vitamin D status in the complex treatment of periodontal pathology is justified.

Thus, at the final stage of scientific research, the frequency of seeding and presence of Prevotella intermedia and Porphyromonas gingivalis in the main group was 18.8% and 12.5%, respectively. Whereas in the same time period, the indicators of the number of people with a high level of saliva contamination in the control group was much higher and amounted to 33.3% and 33.3%, respectively, for both bacteria.

Patients with combined dental and somatic pathologies are recommended to take prophylactic medications based on vitamin D and calcium. It is necessary to prevent interdependence in the development of severe forms of morbidity, in particular, hypothyroidism and periodontitis. It includes the following recommendations: planning-based work to improve oral hygiene knowledge; training in proper oral hygiene skills; regular implementation of necessary preventive and remedial measures; correction of the diet and increasing consumption of foods rich in vitamin D and calcium.

One month later, after periodontitis therapy in combination with elements of supportive treatment in the main group, index indicators continued to decrease more pronounced than in other groups. In this group, the gingival index by the specified period (after 4 weeks) decreased to 0.63 ± 0.027 points; in the second comparison group, the values were higher and amounted to 0.72 ± 0.023 points ($p<0.001$). In the control group, the indicators were even higher – 1.11 ± 0.030 points, respectively ($p<0.001$).

In long-term results, a more pronounced tendency towards an increase in the gingival index was observed in the third control group. In the comparison groups and in the main group there was only a slight increase in values.

Thus, inflammatory periodontal diseases in patients with the endocrine pathology under study are predominantly chronic in nature and, under favorable conditions, are characterized by high activity of both the inflammatory and destructive processes. The dynamics of the decrease in critical values of the GI index after specialized therapy was especially pronounced 3 months after treatment. The results of treatment of inflammatory periodontal diseases using hyaluronic acid showed the most consistent clinical effect in periodontal patients with hypothyroidism. Complex treatment based on the introduction of hyaluronic acid as maintenance therapy has been clinically tested on volunteer patients with hypothyroidism and chronic catarrhal gingivitis and mild periodontitis.

Positive results in subsequent stages of observation continued to increase in the first group, where hyaluronic acid was added to the main treatment. In this group, after therapy, the values of the SBI index, which is known to be an index of gingival sulcus bleeding, decreased as much as possible, and these values did not change over 4, 12, 24 weeks in comparison with other groups.

Among all three compared groups of patients with periodontopathies, the Patient Hygiene Performance (PHP) index was used to evaluate the effectiveness of the agents used in improving oral hygiene over time. In the main group, after the therapy, the PHP index by the end of the study decreased by almost 2.2 times, from 2.58±0.077 to 1.18±0.044 points ($p<0.001$). Changes in the index of oral hygiene effectiveness at the initial and final examination in those examined in the control group decreased from 2.65 ± 0.052 to 1.79 ± 0.071 points, respectively, but in comparison with the indicators in other study groups, the indicators were significantly higher.

At the same time, the rate of salivation at the early and later stages of the studies increased less pronounced when examining female patients.

At subsequent stages (6-12 months), after carrying out comprehensive measures to correct the identified pathological processes in the oral cavity, in particular, in periodontal tissues, there was a certain improvement in the situation. So, immediately before treatment, in women from the control group, the rate of salivation was 1.45±0.01 ml/min, and two weeks after professional hygiene the average value of the studied indicator increased compared to the initial value and amounted to 1.76±0.02 ml/min (p_1<0.0001).

The main indicators of the therapeutic and preventive effects of hyaluronic acid were the data from control tests carried out in the laboratory, which were obtained 4 weeks after treatment, and immediately the clinical manifestations characteristic of inflammatory processes in the periodontium disappeared.

When conducting a course of basic treatment in combination with hyaluronic acid, patients with periodontitis should note the range of action of the drug used, which is characterized by minimal activity against aerobes and anaerobes. Using the analysis of bacteriological screening, the high efficiency of this drug relative to pathogenic and opportunistic microflora was revealed when using its usual concentration.

Thus, when examining patients with mild periodontitis and gingivitis, before the start of treatment, representatives of periodontopathogenic microorganism species were isolated in significant numbers. After anti-inflammatory therapy with the use of hyaluronic acid for 14 days, the qualitative and quantitative composition of oral fluid bacteria changed markedly.

After completion of treatment within the specified period in the main group in mixed saliva, the frequency of isolation of the main pathogens A.actinomycetemcomitans and P.intermedia responsible for the development of the most severe forms of periodontal disease significantly decreased. At the same time, the frequency of isolation of the latter at the initial stage of research and later on decreased by 3-6.5 times, respectively. Thus, the incidence of P.intermedia immediately after treatment was 15.4±10.01%, and after a month it decreased even more and was fixed at 7.7±7.39%, with an initial rate before treatment of 46.2±13.83%, (p<0,05). According to the results of the second

stage, that is, bacteriological studies, the composition of microorganisms in the oral cavity, both qualitative and quantitative, changed in patients suffering from thyroid disease. At the same time, as a result of determining the species composition of bacteria in mixed saliva, it was found that in patients with hypothyroidism, inflammatory and destructive disease of periodontal tissues was provoked mainly by various associations of periodontopathogenic microorganisms. Among them, it was more often possible to record the presence of P. gingivalis and P. intermedia. In the control group, the incidence of Candida albicans immediately after completion of treatment decreased to 25.0±12.50%, with 41.7±14.23% of the indicators before treatment.

In patients of the main group who received hyaluronic acid as an additional maintenance therapy as part of complex periodontal therapy, there was a progressive increase in the microbiocenosis of the oral fluid (S. Epidermidis) - 23.1 ± 11.69% - an indicator at 14 days after treatment with 30.8±12.80% of the values for this bacterium identified after a month.

One week after treatment using a traditional antiseptic, the number of S.aureus and P.intermedia significantly decreased in all patients compared to the initial values. Pathogenetically important was a significant decrease after a month in the quantitative indicators of Candida albicans yeast-like fungi, the values for which decreased by almost double: in comparison group values changed from 72.7±14.43% to 27.3±13.43% ($p<0.05$). A month after treatment, there was a decrease in the number of S.aureus by 33.6% ($p<0.05$), P.intermedia – by 83.3% ($p<0.001$) and Candida albicans – by 50.0% ($p<0.01$).

In case of mild chronic generalized periodontitis and catarrhal gingivitis, a decrease in the amount of normal oral flora and, at the same time, replacement of the coccal flora with gram-negative fusobacteria can be detected. It is also necessary to note the presence of opportunistic pathogens and an increase in the number of A. actinomycetemcomitans in the oral cavity, which continue to prevail with increasing severity of periodontal pathology. With moderate periodontitis, a decrease in the number of representatives of gram-negative flora is observed, and the main spectrum of oral microflora is represented by opportunistic and pathogenic cocci.

The results of microbiological studies of the oral cavity showed a change in the ratio of quantitative indicators of aerobic and anaerobic microorganisms depending on the severity of periodontitis and gingivitis. At the same time, gram-negative rod-shaped flora and actinomycetes are almost completely replaced by cocci, fusobacteria and fungal infections, that is, conditionally pathogenic and pathogenic flora. These studies showed that in the group of patients with mild chronic generalized periodontitis, an increase in secondary resident flora was most often observed.

Fusobacteria dominated among gram-negative anaerobic microorganisms, and their concentration in saliva exceeded those detected in healthy individuals. In addition to resident representatives, Streptococcus pyogenus, Streptococcus pneumoniae and Enterococcus faecalis are sown for mild periopathologies. It is important to note that correction of oral microbiocenosis in patients with periodontitis is a necessary addition to the treatment regimen for the underlying pathology itself. This ensures the elimination of the periodontopathogenic situation and a significant increase in the comfort of life of this population.

The most promising in this regard will be drugs that do not have toxicity or allergic side effects. But at the same time, they should also be easily absorbed and have a pronounced antibacterial effect.

Consequently, the inclusion of hyaluronic acid in the treatment regimen revealed two important characteristic trends in the microbiocenosis of the oral cavity in patients with hypothyroidism: frequency of individuals with a high level of contamination with representatives of periodontopathogenic bacteria and microscopic fungi of the genus Candida sharply decreased. Additionally, quantitative indicators of some representatives of the stabilizing normal microflora such as streptococci of the oral cavity normalized.

CONCLUSIONS

1. Among patients with hypothyroidism, the incidence of periodontal disease was noted at 96%. In general, bleeding was observed in 6.00±1.94 cases, dental calculus - 44.7±4.06 cases, periodontal pockets: 4-5 mm deep - 28.0±3.67 cases, 6 mm and deeper - 17.3±3.09 cases. Along with hypothyroidism, the periodontal index exceeded the control indicator by 1.6 times ($t=70.4$, $p<0.001$), the gingival index - by 1.8 times ($t=23.4$, $p<0.001$). [1]

2. In patients with hypothyroidism, chronic generalized mild periodontitis was diagnosed 73.7% less often ($p<0.01$), and moderate and severe cases, respectively, by 50.6% ($p<0.01$) and 66.8% ($p<0.01$) more often than in patients without hypothyroidism. Patients with hypothyroidism were characterized by hyposalivation, which was expressed by a reduced rate of salivation and buffering capacity of saliva. [2,4]

3. Along with hypothyroidism, a low level of sIgA, an increased content of IgA and IgG, accumulation of MDA, a decrease in the amount of SOD and catalase were noted in the oral fluid, which represents a risk factor for the development of inflammation and immunopathological reactions in periodontal tissues. [6, 7, 10]

4. The inclusion of a vitamin-mineral complex as an additional supportive treatment contributed to a decrease in the Russel periodontal index (25.8%, $p<0.05$), Silness-Loe gingival index (60.5%, $p<0.001$), periodontal pocket depth index (25.2%, $p<0.001$), BOP index (80.5%, $p <0.001$), PMA index (65.3%, $p<0.05$); reduced seeding of Prevotella intermedia (66.6%) and Porphyromonas gingivalis (83.3%); improvement of the pH index of mixed saliva (2.7%) and the state of the functions of the salivary glands (11.9%). [4, 5]

5. Applications of hyaluronic acid improve the existing imbalance between pro-oxidants (MDA) and antioxidants (SOD, catalase) in the oral fluid, have a positive effect on the dynamics of local immunity (sIgA), oral microbiota: after 30 days of treatment the number of S. aureus decreased by 33.6% ($p <0.05$), P.intermedia – by 83.3% ($p<0.001$) and Candida albicans – by 50.0% ($p<0.01$). [3, 8, 9]

PRACTICAL RECOMMENDATIONS

1. Taking into account the results of the clinical and laboratory research, effective methods for the timely identification of pathological disorders in the oral cavity and treatment of mild and moderate periodontitis in patients with hypothyroidism have been proposed.

2. In the treatment of gingivitis and periodontitis of mild and moderate forms in patients with hypothyroidism, it is advisable to include applications of hyaluronic acid for 14 days, which will significantly positively change the outcome of treatment of periodontitis and gingivitis, as well as significantly reduce the number of complications and relapses.

3. For patients with hypothyroidism and vitamin D deficiency, in order to correct periodontal diseases, it is recommended to include a calcium + vitamin D supplement in complex therapy in a dose according to individual indicators.

4. Patients with hypothyroidism are a group with a high probability of developing severe periodontitis and, according to indications, such patients are recommended to take prophylactic medications based on vitamin D and calcium, as well as the use of hyaluronic acid.

List of published scientific papers on the topic of the dissertation:

1. Алиева Л.А. К проблеме патологии щитовидной железы в пародонтологии // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, 2019, № 4, c.18-23.
2. Рагимов Ч.Р., Гусейнова Т.Г., Алиева Л.А. Лечебно-профилактические особенности заболеваний пародонта у больных гипотиреозом // – Kyiv: Сучасна Стоматологія, 2020, № 1(100), с.34-38.
3. Алиева Л.А. Лечение и профилактика воспалительных заболеваний пародонта препаратами на основе гиалуроновой кислоты // – Полтава: Вісник проблем біології і медицини, 2020, Выпуск 1 (155), с.347-351.
4. Алиева Л.А. Анализ стоматологического статуса и его коррекция у пациентов с гипотиреозом // – Bakı: Azərbaycan Tibb Jurnalı, 2020, № 2, c.19-24.
5. Алиева Л.А. Состояние тканей пародонта и эффективность лечебно-профилактических мер в зависимости от тиреоидного статуса организма // – Bakı: "Sağlamlıq" Elmi-praktik jurnal, 2020, № 4, c.91-96.
6. Алиева Л.А. Коррекция стоматологического статуса у больных гипотериозом // Наука и инновации-современные концепции (сборник научных статей по итогам работы Международного научного форума) том 2, Москва, 2020, с.64-65.
7. Гусейнова Т.Г., Алиева Л.А., Гасымова З.В., Султанова Н.Н. Повышение эффективности лечения и профилактики пародонта на фоне медикаментозной коррекции недостаточности витамина D // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, 2021, №3, c.154-162.
8. Алиева Л.А., Юсубова Ш.Р., Мамедов Ф.Ю. Влияние гиалуроновой кислоты на состояние иммунитета и антиоксидантную активность полости рта // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, 2021, № 4, c.59-64.
9. Алиева Л.А. Повышение эффективности лечения заболеваний пародонта с применением гиалуроновой кислоты //

Azərbaycan Tibb Universitetinin yaradılmasının 90, Azərbaycanda Ali Əczaçılıq təhsilinin 80 illik yubileylərinə həsr edilmiş "Əczaçılığın müasir problemləri" mövzusunda V Beynəlxalq Elmi Konqresin materialları, Bakı, 2021, c.314-316.

10. Алиева Л.А. Повышение эффективности лечения воспалительных заболеваний пародонта у больных с дисфункцией щитовидной железы // – Bakı: Qafqazın Stomatoloji Yenilikləri, 2022-2023, №27, c.90-91.

List of abbreviations

25(OH)D	–	25-hydroxycholecalciferol
BOP	–	Bleeding on Probing
DMFT	–	Decayed Missing Filled Teeth
CPITN	–	Community Periodontal Index of Treatment Needs
SOD	–	superoxide dismutase
GI	–	Gingival Index
IgA	–	Immunoglobulin A
IgG	–	Immunoglobulin G
MDA	–	malondialdehyde
PHP	–	Patient Hygiene Performance Index
PMA	–	papillary-marginal-alveolar index
SBI	–	Sulcular Bleeding Index
sIgA	–	Secretory Form of Immunoglobulin A
WHO	–	World Health Organization

The defense will be held on «15» May 2024 at «14:00» at the meeting of the Dissertation council ED 2.50 operating at Azerbaijan Medical University.

Address: AZ 1022 Baku city, A.Gasimzade str. 14.(conference hall).

The dissertation is accessible at the Azerbaijan Medical University library.

Electronic versions of dissertation and its abstract are available on the official website of the Azerbaijan Medical University (www.amu.edu.az).

Abstract was sent to the required addresses on «08» April 2024.

Signed for print : 02.02.2024
Paper format: 60 x 84 1/16
Volume: 37.900 characters
Number of hard copies: 20