

9. Kruk ME, Gage AD, Joseph NT, Danaei G, García-Saisó S, Salomon JA. Mortality due to low-quality health systems in the universal health coverage era: a systematic analysis of amenable deaths in 137 countries. *Lancet*. 2018; 392:2203–2212. [https://doi.org/10.1016/S0140-6736\(18\)31668-4](https://doi.org/10.1016/S0140-6736(18)31668-4)
10. Libby P. History of discovery: inflammation in atherosclerosis. *Arterioscler Thromb Vasc Biol*. 2012; 32(9):2045–2051. <https://doi.org/10.1161/ATVBAHA.108.179705>
11. Libby P, Hansson GK, Lichtman AH. Immune effector mechanisms implicated in atherosclerosis: from mice to humans. *Immunity*. 2013;38(6):1092–104. <https://doi.org/10.1016/j.immuni.2013.06.009>
12. Liu DJ, Peloso GM, Yu H, Butterworth AS, Wang X, Mahajan A et al. Exome-wide association study of plasma lipids in >300,000 individuals. *Nat Genet*. 2017;49(12):1758–1766. <https://doi.org/10.1038/ng.3977>.
13. Perrins C.J., Bobryshev Y.V. Current advances in understanding of immunopathology of atherosclerosis. *Virchows Arch*. 2011;458(2):117–23. <https://doi.org/10.1007/s00428-010-1006-5>.
14. Shi N, Chen SY. Smooth muscle cell differentiation: model systems, regulatory mechanisms, and vascular diseases. *J Cell Physiol*. 2016;231(4):777–87. <https://doi.org/10.1002/jcp.25208>
15. Tabas I., Lichtman AH. Monocyte-macrophages and T cells in atherosclerosis. *Immunity*. 2017;47(4):621–634. doi: 10.1016/j.immuni.2017.09.008.

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## INCREASING THE EFFICIENCY OF TREATMENT OF INFLAMMATORY PERIODONTAL DISEASES IN PATIENTS WITH THYROID DISEASES

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A comprehensive periodontal examination and questionnaire survey of 150 people suffering from thyroid dysfunction and chronic generalized periodontitis (the average age of patients was  $31.6 \pm 0.46$  years) and 150 practically healthy persons of the same age and sex were carried out. The level of MDA concentration after completion of the course of basic therapy in all groups was  $0.71 \pm 0.03$  nmol/ml,  $1.30 \pm 0.03$  nmol/ml, and  $2.89 \pm 0.15$  nmol/ml, respectively, in the main group, the control group and the comparison group. The results of biochemical studies showed a less pronounced trend in comparison with the main group of patients in the normalization of the content of S-IgA immunoglobulins –  $0.46 \pm 0.023$  mg/l. The fact of a more pronounced increase in the amount of sIgA in saliva after the use of hyaluronic acid is associated with a significant activation of immunological processes in the oral cavity.

**Key words:** periodontal disease, hypothyroidism, saliva, immunity, antioxidant system, hyaluronic acid

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## ПІДВИЩЕННЯ ЕФЕКТИВНОСТІ ЛІКУВАННЯ ЗАПАЛЬНИХ ЗАХВОРЮВАНЬ ПАРОДОНТА У ПАЦІЄНТІВ ІЗ ЗАХВОРЮВАННЯМИ ЩИТОПОДІБНОЇ ЗАЛОЗИ

Проведено комплексне пародонтологічне обстеження і анкетування 150 осіб, які страждають порушеннями функції щитоподібної залози і хворіють на хронічний генералізований пародонтит (середній вік пацієнтів склав  $31,6 \pm 0,46$  років) і 150 практично здорових осіб аналогічного віку та статі. Рівень концентрації МДА після завершення курсу базової терапії у всіх групах дорівнював  $0,71 \pm 0,03$  нмоль/мл,  $1,30 \pm 0,03$  нмоль/мл і  $2,89 \pm 0,15$  нмоль/мл, відповідно до основної, контрольної групи і групи порівняння. Результати біохімічних досліджень показали менш виражену в порівнянні з основною групою пацієнтів тенденцію до нормалізації вмісту імуноглобулінів S-IgA -  $0,46 \pm 0,023$  мг/л. Факт більш вираженого збільшення в слині кількості sIgA після застосування гіалуронової кислоти пов'язаний зі значною активізацією імунологічних процесів в порожнині рота.

**Ключові слова:** захворювання пародонту, гіпотиреоз, слина, імунітет, антиоксидантна система, гіалуронова кислота

*The work is a fragment of the doctoral thesis: "Role of general somatic diseases in increasing the prevalence and intensity of major dental diseases and improvement of treatment and prophylactic measures"*

The modern concept of the etiology and pathogenesis of dental diseases considers the systemic-somatic risk factor as one of the leading among a rather extensive complex of mechanisms that determine the development of pathological processes of an inflammatory and destructive nature in the organs and tissues of the oral cavity [1].

In the course of scientific research, some etiopathogenetic aspects of periodontal diseases of an inflammatory and destructive nature and dental caries were identified and, ultimately, a close relationship and interdependence of diseases of the oral cavity with endocrine pathologies was determined [2]. A number of systemic immune disorders and the destructive effect of free radicals, including at the local level, with a lack of thyroid hormones, which have immunostimulating and corrective properties, have also

been established [3]. One of the main requirements for the complex therapy of periodontal disease in patients with somatic pathology is the individualization of therapeutic and prophylactic agents and methods that provide for the choice of optimal and timely therapeutic and prophylactic methods at the general and local levels, especially the initial stage of the development of pathology, which prevents the occurrence of a process in the bone and thus significantly improves the quality of life of patients [7]. Creation and introduction of funds with different percentages of hyaluronic acid, superior in their properties to traditional ones, provided there is sufficient information about the mechanism of influence of this drug on the pathogenetic links of the main dental diseases and the methodological features of its use, it opens up wide opportunities for their use in practical periodontics [4, 10]. All of the above determines the importance of conducting clinical and laboratory studies to assess the effectiveness of the use of hyaluronic acid in the treatment and prevention of periodontal disease in patients with thyroid dysfunction.

**The purpose** of the study was to assess the dynamics of biochemical parameters in the oral cavity of patients with hypothyroidism and periodontal disease before and after the use of hyaluronic acid.

**Materials and methods.** A comprehensive dental examination and questioning of 150 people with thyroid dysfunction and chronic generalized periodontitis (the average age of patients was  $31.6 \pm 0.46$  years) and 150 people in the control group of the same age and sex were carried out. The study was carried out in 2018–2020 at the Department of Maxillofacial Surgery of the Azerbaijan Medical University, as well as the Specialized Endocrinology Center and a private dental clinic in Baku. The patients were divided into 3 groups depending on the method of therapy. In the 1st group,  $n=13$  (main group), the scheme of maintenance therapy in the main group was as follows: the examined patients were injected with hyaluronic acid turundas in the area of the periodontal tissues for 14 days. In group II, the comparison group ( $n=11$ ), a traditional antiseptic was used, all patients in the oral cavity were removed tartar and gums were applied with a traditional antiseptic, chlorhexidine solution. The local treatment in the control group III ( $n=12$ ) included the removal of dental plaque, closed curettage as part of individual oral hygiene. The exposure time with the drug was 5–10 minutes. All patients underwent: oral hygiene training, professional hygiene, complete sanitation. During the control dental examinations, the state of the periodontal tissues was determined by determining the hygienic index (HI) Silness – Loe (S – L, 1964), and the periodontal index – PI (A.L. Russel, 1956, 1967).

Biochemical analysis of the oral fluid was performed before and after completion of the course of basic therapy. The state of pro-inflammatory enzymes was judged by the level of malondialdehyde (MDA) in saliva, that is, by the quantitative indicators of intermediate products that react with thiobarbituric acid. The activity of SOD and catalase was used to judge the activity of the antioxidant defense system before and after the use of hyaluronic acid. The quantitative determination of immunoglobulins IgA, IgG and sIgA in saliva was carried out using the method of G. Mancini, A.O. Carbonaro (1965) – radial immunodiffusion, and the concentration was expressed in mg/l.

In the course of statistical processing, the arithmetic mean (M) and the mean error of the mean value (m) were estimated. P – the statistical significance of the difference relative to before treatment was determined by the paired Wilcoxon test and the Mann-Whitney U-test for independent samples. A significant difference between the compared groups was considered at  $p < 0.05$ . The resulting material was

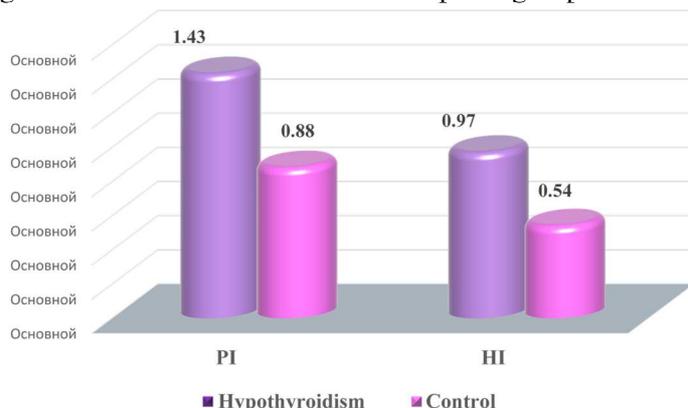


Fig. 1. Index assessment of the periodontal condition in a comparative aspect ( $n=300$ )

processed using a standard software package (Microsoft Excel, Statistica for Windows v. 7.0).

**Results of the study and their discussion.** According to the results of the statistical analysis of the data of periodontal indices in the group without endocrine pathology, the obtained data corresponded to the development of a mild inflammatory reaction in the periodontal tissues in response to the deterioration of the hygienic state of the oral cavity (fig. 1).

Thus, the indices of the Russell index in this experimental group were  $0.88 \pm 0.005$  points, with  $1.43 \pm 0.006$  points, corresponding to the value of the index in the main group ( $p=0.0001$ ). That is, in practically healthy individuals, the value of the periodontal index PI was almost by 1.5 times lower than in patients with hypothyroidism ( $p=0.0001$ ). Thus, in the control group, the studied indices are significantly lower than in the group of patients with thyroid pathology. Moreover, in patients with hyperthyroidism, the

gingival index was much higher than in the control group  $0.97 \pm 0.016$  points and  $0.54 \pm 0.009$  points, respectively ( $p=0.0001$ , at  $t=21.94$ ), that is, in patients with background pathology, the course of the inflammatory process is more intense.

According to the results of a survey of 150 patients with hypothyroidism, it was revealed that one dentist constantly monitors the majority of the examined, less often patients are found who visit different

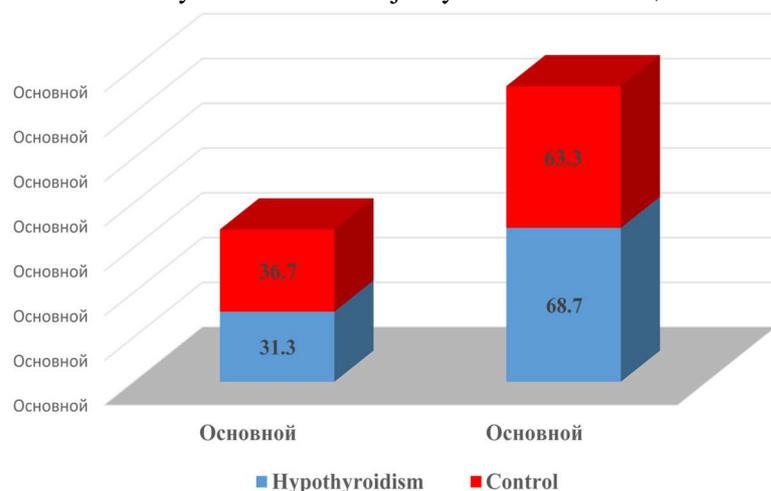


Fig. 2. Frequency of visits to the dentist among the surveyed persons, %

specialists. 68.7 % of the interviewed patients with endocrine pathology noted that they visit a dentist twice a year (fig. 2). Almost a similar picture was observed when questioning individuals in the control group without background pathology. In two times less number of cases, respondents visited the dentist once a year or even less often – 31.3 % and 36.7 %, respectively, in the main and control groups.

The study of the oral fluid in patients before the start of treatment and prophylactic measures showed

that in the oral cavity with the development of the inflammatory process in the periodontal tissues and against the background of 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, indicated a pronounced intensification of the process of free radical oxidation of lipids (table 1).

□bl□1

#### Biochemical parameters of oral fluid in patients during treatment

Groups	Date	Indicators		
		MDA, nmol/ml	SOD, %	Catalase activity, $\mu\text{at} / \text{l}$
Group 1, n=13	before treatment	$1.08 \pm 0.05$	$42.4 \pm 0.26$	$43.1 \pm 0.29$
	after treatment	$0.71 \pm 0.03$	$45.3 \pm 0.18$	$46.2 \pm 0.20$
	P	0.0001	0.0001	0.0001
Group 2, n=12	before treatment	$1.97 \pm 0.05$	$34.6 \pm 0.68$	$36.1 \pm 0.45$
	after treatment	$1.30 \pm 0.03$	$37.2 \pm 0.36$	$38.7 \pm 0.64$
	P	0.0001	0.0042	0.0036
Group 3, n=11	before treatment	$4.04 \pm 0.24$	$23.5 \pm 0.31$	$22.3 \pm 0.44$
	after treatment	$2.89 \pm 0.15$	$40.2 \pm 0.45$	$34.5 \pm 0.38$
	P	0.0007	0.0001	0.0001

Note: P is the statistical significance of the difference relative to pre-treatment (paired Wilcoxon test)

The most favorable situation was observed in patients with catarrhal gingivitis and mild periodontitis in the study group, where the level of peroxidation was the lowest in comparison with the control group and the comparison group. So the level of MDA after completion of the course of basic therapy in groups was  $0.71 \pm 0.03$  nmol/ml,  $1.30 \pm 0.03$  nmol/ml and  $2.89 \pm 0.15$  nmol/ml, respectively, in the main, control group and in the comparison group. In addition, the same patients had a high concentration of lipid peroxidation products and a decreased level of antioxidant defense enzymes in the oral cavity before the start of treatment ( $p < 0.05$ ).

The results of the treatment of periodontitis indicated a significant increase in the level of catalase in the oral fluid against the background of the use of traditional therapy from  $22.3 \pm 0.44$   $\mu\text{at}/\text{l}$  to  $34.5 \pm 0.38$   $\mu\text{at}/\text{l}$  ( $p < 0.05$ ). Patients of the other two experimental groups were no exception. The use of hyaluronic acid makes it possible to introduce some positive changes in the process of free radical oxidation itself and can lead to an increase in the activity of metabolic and reparative processes in the periodontal tissues, to a certain extent, it can reduce the intensity of the above processes. The positive effect of hyaluronic acid on oxidative stress was accompanied, according to the patients themselves, by a significant improvement in the clinical picture in the complex treatment and prevention of inflammatory periodontal diseases against the background of general somatic pathology. According to the preliminary laboratory data obtained, a

certain pathogenetic justification for the introduction of the drug into the complex treatment of inflammatory and destructive periodontal diseases was revealed, which makes further study of the effectiveness of the use of hyaluronic acid in dentistry very important, both from a scientific and practical point of view. Biochemical studies of saliva and the content of immunoglobulins in it in patients of all three groups with somatic pathology recorded a significant decrease in sIgA indices and an increase in IgG in the oral fluid (Table 2), which indicated a weakening of their immunological reactivity.

Table 2

**Content of immunoglobulins in saliva before and after treatment**

Parameter		Main group n=13	Group Comparison n=11	Control group n=12
IgA	before treatment	0.39±0.021	0.23±0.016	0.41±0.023
	after treatment	0.31±0.015	0.18±0.012	0.34±0.017
	P	0.0037	0.0228	0.0265
S-IgA	before treatment	0.36±0.027	0.34±0.019	0.32±0.016
	after treatment	0.51±0.019	0.42±0.022	0.46±0.023
	P	0.0001	0.0092	0.0001
IgG	before treatment	0.67±0.031	0.68±0.030	0.68±0.021
	after treatment	0.56±0.027	0.54±0.021	0.43±0.018
	P	0.0073	0.0016	0.0001

Note: P is the statistical significance of the difference relative to pre-treatment (paired Wilcoxon test)

The use of hyaluronic acid as a means of anti-inflammatory and supportive therapy contributed to a sharp increase in sIgA and a correction of the IgG content in saliva and restoration, to a certain extent, of the barrier function of organs and tissues of the oral cavity. The S-IgA level after professional oral hygiene and the traditional antiseptic 0.05 % chlorhexidine bigluconate increased from 0.34±0.019 mg/L to 0.42±0.022 mg/L (p=0.0092).

A decrease in the content of class G immunoglobulin in the oral fluid from 0.68±0.030 mg/l and to 0.54±0.021 mg/l, respectively, before and after the end of the application of the traditional antiseptic (p=0.0016). The results of biochemical studies showed a less pronounced trend in comparison with the main group of patients in the normalization of the content of immunoglobulins S-IgA – 0.46±0.023 mg/l, in the control group.

According to the results of clinical and laboratory studies, the presence of endocrine pathology negatively affects the functional state of the organs and tissues of the oral cavity, as evidenced by the indicators of the periodontal index, which characterizes the degree of spread of the inflammatory process to the soft and hard periodontal tissues, and changes in some biochemical parameters. Thus, in the patients examined by us against the background of hypothyroidism, changes in the indices of local immunity and antioxidant protection of the oral cavity were revealed. As the author emphasizes, such violations also occur at the system level [1]. In our opinion, the main predisposing pathogenetic factor in the development of dental diseases with hypothyroidism is the multifactorial effect of somatic pathology on human metabolism, which, as confirmed by some authors, leads to a slowdown in the rate of bone resorption and bone formation, stimulating both osteoblastic and osteoclastic activity. They found that with a decrease in the level of thyroid hormones, the activity of both osteoblasts and osteoclasts decreases. [nine]. Timely implementation of sanitation measures with the removal of dental deposits, filling of carious cavities, removal of the roots of decayed teeth and the appointment of effective hygiene products in the course of complex treatment provides a relative normalization of local immunity and regression of clinical symptoms of diseases. But it is important to cite the opinions of scientists that often in inflammatory periodontal diseases to suppress periodontal pathogenic microflora of dental plaque, antiseptics are used, broad-spectrum antimicrobial substances that do not have a selective effect on microorganisms and cause protein denaturation [8]. It should be noted that under favorable conditions these agents are protoplasmic poisons and can have toxic-allergic side effects. On the basis of index data obtained in the course of clinical trials, it can be concluded that it is advisable to prescribe complex treatment for periodontitis using hyaluronic acid in patients with hypothyroidism. The normalization of histochemical parameters in animals, which was achieved by the author after four and six weeks of experimental studies, may indicate an increase in compensatory mechanisms in tissues and an increase in immunological reactivity after using this drug [5]. This fact was confirmed by the results of our biochemical studies to identify the dynamics of changes in the quantitative indicators of S-IgA, which significantly increased after the use of hyaluronic acid in complex periodontal treatment. An important

point, according to some authors, is the effectiveness of the use of hyaluronic acid in periodontal surgery [6]. The prospect of further research is confirmation of the long-term effectiveness of our proposed method of treating periodontal diseases combined with endocrine pathology on the basis of clinical, immunological and microbiological research methods in the matter of maximally long-term normalization of dental disorders caused by concomitant pathology and preservation of the obtained effect.

### Conclusion

A high level of need for patients with hypothyroidism in dental care was found due to the high intensity of periodontal diseases ( $PI=1.43\pm 0.006$ , versus the values of the same index in the control group  $0.88\pm 0.005$ ). The inclusion of hyaluronic acid in the complex of treatment of chronic periodontitis improves the indices of local immunity of the oral cavity. The S-IgA level in the main group increased by almost 1.3 times.

### References

1. Biktagirova EM. Biokhimicheskiye i immunologicheskiye markery khronicheskogo limfotsitarnogo tireoidita. *Biomeditsinskaya khimiya*. 2016; 62(4): 458–465. DOI: 10.18097/PBMC20166204458 [in Russian]
2. Satygo Ye A, Shevchenko LM, Vasilyeva NV, Rakhmatullin RR. Otsenka effektivnosti primeneniya v stomatologii balzama opolaskivatelya na osnove gialuronovoy kisloty u kuryashchikh patsiyentov. *Parodontologiya*. 2016; 21(4): 40–43. [in Russian]
3. Khaydarov AM, Rizayev EA. Rasprostranennost zabolevaniy parodonta sredi detskogo i vzroslogo sloyev naseleniya prozhivayushchikh v gorodakh s razlichnoy ekologicheskoy obstanovkoy. *Journal of biomedicine and practice*. 2016, vol. 1, issue 1, pp. 31–35. DOI:10.26739/2181-9300-2016-1-6 [in Russian]
4. Casale M, Moffa A, Vella P., Sabatino L., Capuano F., Salvinelli B, et al. Hyaluronic acid: Perspectives in dentistry. A systematic review. *International Journal of Immunopathology and Pharmacology*. 2016 Dec; 29(4):572–582. <https://doi.org/10.1177/0394632016652906>
5. Gontiya G and Galgali SR (2012) Effect of hyaluronan on periodontitis: A clinical and histological study. *Journal of Indian Society of Periodontology* 16: 184–192.
6. Kumar R, Srinivas M, Pai J, et al. (2014) Efficacy of hyaluronic acid (hyaluronan) in root coverage procedures as an adjunct to coronally advanced flap in Millers Class I recession: A clinical study. *Journal of Indian Society of Periodontology* 18: 746–750.
7. Pippi R. Post-surgical clinical monitoring of soft tissue wound healing in periodontal and implant surgery. *Int J Med Sci*. 2017; 14: 721–728 DOI: 10.7150/ijms.19727
8. Saimir Heta and Ilma Robo. The Side Effects of the Most Commonly Used Group of Antibiotics in Periodontal Treatments *Med Sci (Basel)*. 2018 Mar; 6(1): 6–11.
9. Siru R, Alfonso H, Chubb S, Golledge J, Flicker L, et al. (2018) Subclinical thyroid dysfunction and thyroid hormones are not associated with bone turnover markers or incident hip fracture in older men. *Clin Endocrinol* 89: 93–99.
10. Tejaswin P, Srinivas M, Swamy N, Aluru S, Chakrapani S, Appaiah C. B. Local delivery of hyaluronan 0.8% as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A clinical and microbiological study. *Journal of Indian Society of Periodontology*. Jan-Feb 2015;19(1):37–42. DOI: 10.4103/0972-124X.145807

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