JUSTIFICATIVA PARA O USO DO COMPLEXO TERAPÊUTICO E PROFILÁTICO PARA EVITAR INTOLERÂNCIA A ACRILATOS EM PACIENTES COM HIPERFUNÇÃO DAS GLÂNDULAS TIREÓIDES**RATIONALE FOR THE USE OF THERAPEUTIC AND PROPHYLACTIC COMPLEX TO PREVENT INTOLERANCE TO ACRYLATES IN PATIENTS WITH HYPERFUNCTION OF THE THYROID GLANDS****ОБОСНОВАНИЕ ПРИМЕНЕНИЯ ЛЕЧЕБНО-ПРОФИЛАКТИЧЕСКОГО КОМПЛЕКСА ДЛЯ ПРЕДУПРЕЖДЕНИЯ НЕПЕРЕНОСИМОСТИ К АКРИЛАТАМ У БОЛЬНЫХ С ГИПЕРФУНКЦИЕЙ ЩИТОВИДНОЙ ЖЕЛЕЗЫ**

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RESUMO

Este estudo é dedicado à análise do efeito da prótese removível de acrílico sobre os tecidos mucosos e duros da cavidade oral de pacientes com hipertireoidismo e, também, para justificar a aplicação de uma gama de medidas curativas e profiláticas baseadas na preparação "Endonorm" para prevenção de eventos de intolerância em pacientes com patologia mencionada. As alterações morfológicas e funcionais da glândula tireóide afetam o estado geral do corpo humano, incluindo os tecidos da cavidade oral, e essas deficiências geralmente se manifestam pela perda precoce de dentes devido a cárie e doenças periodontais. As manifestações orais da tireotoxicose incluem aumento da suscetibilidade à cárie, doença periodontal, aumento do tecido extraglandular da tireóide, osteoporose maxilar ou mandibular, dentição acelerada e síndrome da boca ardente. Este problema nesses pacientes, em particular aqueles que sofrem de hiperfunção da glândula tireóide, deve ser resolvido por meio de terapia medicamentosa complexa para aumentar a resistência e reduzir o nível de sensibilização do corpo. "Endonorm" é uma mistura de extratos vegetais secos de *Potentilla alba Linnaeus*, preparado de acordo com tecnologia especial, o principal componente ativo do produto é a Albinina. Objetivo de estudar os indicadores de atividade semelhante à tripsina da saliva mista em pacientes com hiperfunção da glândula tireóide, cujas próteses foram fabricadas pelo método padrão de compressão e usando medidas terapêuticas e profiláticas propostas. Após a definição da aplicação de próteses removíveis, o aumento da atividade enzimática da saliva em 17%, em comparação com os índices, anteriores ao início da prótese. Estabeleceu que a faixa de medidas curativa e profilática proposta permite evitar o risco de desenvolvimento de eventos de intolerância ao acrilato e normalizar os índices estudados 1 mês após a prótese.

Palavras-chave: hipertireoidismo (hiperfunção da glândula tireóide), alergia, prótese removível.

ABSTRACT

This investigation is devoted to the analysis of acrylic removable denture's effect on the mucous and hard tissues of the oral cavity of patients with hyperthyroidism and, also, to rationale for application the curative and prophylactic range of measures based on the preparation "Endonorm" for precaution of events of intolerance of patients with mentioned pathology. Morphological and functional changes in the thyroid gland

affect the general state of the human body, including tissues of the oral cavity, and these impairments usually manifest by the early loss of teeth due to caries and periodontal diseases. Oral manifestations of thyrotoxicosis include increased susceptibility to caries, periodontal disease, enlargement of extraglandular thyroid tissue, maxillary or mandibular osteoporosis, accelerated teething, and burning mouth syndrome. This problem in such patients, in particular, those suffering from hyperfunction of the thyroid gland, should be resolved by means of complex medicinal therapy to increase resistance and reduce the level of body sensitization. "Endonorm" is a mixture of dry vegetable extracts of white cinquefoil, prepared according to special technology, the main active component of the product is Albinin. Purpose of studying the indicators of trypsin-like activity of mixed saliva in patients with hyperfunction of the thyroid gland, whose dentures were manufactured by standard compression method, and by using proposed therapeutic and prophylactic measures. After the applying of removable dentures was defined, the increase of saliva's enzyme activity on 17% as compared with indices, which was before the beginning of the prosthesis. It established that the proposed curative and prophylactic range of measures permits to prevent the risk of development of events of acrylate intolerance and to normalize the studied indices on 1 month after the prosthesis.

Keywords: *hyperthyroidism (hyperfunction of the thyroid gland), allergy, removable denture.*

АННОТАЦИЯ

Данное исследование посвящено изучению влияния акриловых съемных протезов на слизистую и твердые ткани полости рта у больных с гиперфункцией щитовидной железы и обоснованию применения лечебно-профилактического комплекса на основе препарата «Эндонорм» для профилактики явлений непереносимости у больных с указанной патологией. Морфофункциональные изменения щитовидной железы оказывают влияние как на организм человека в целом, так и на ткани полости рта в частности, что проявляется ранней утратой зубов вследствие кариеса и заболеваний пародонта. К проявлениям тиреотоксикоза в полости рта относятся: повышенная восприимчивость к кариесу, пародонтит, увеличение экстраглангулярной ткани щитовидной железы, верхнечелюстной или нижнечелюстной остеопороз, ускоренное прорезывание зубов и синдром жжения в полости рта. Данная проблема у таких больных, в частности страдающих гиперфункцией щитовидной железы, должна быть решена путем комплексной терапии с применением медикаментозных препаратов для повышения резистентности и снижения уровня сенсибилизации организма. Препарат «Эндонорм» представляет собой смесь произведенных по особой технологии сухих растительных экстрактов лапчатки белой (лат. *Potentilla alba Linnaeus*), основным действующим началом которой является субстанция Альбинин. Цель исследования: изучить показатели трипсиноподобной активности смешанной слюны у больных с гиперфункцией щитовидной железы, съемные протезы которым были изготовлены традиционным компрессионным методом и с применением предлагаемого лечебно-профилактического комплекса. Было выявлено увеличение ферментативной активности слюны после наложения съемных протезов на 17 % по сравнению с показателями до начала протезирования. Установлено, что предлагаемый лечебно-профилактический комплекс позволяет предупредить риск развития явлений непереносимости к акрилатам и нормализовать изучаемые показатели через 1 месяц после протезирования.

Ключевые слова: *гиперфункция щитовидной железы, аллергия, съемные протезы.*

1. INTRODUCTION

On the features of the structure and function of the thyroid gland.

The thyroid gland (glandula thyroidea) is a gland of internal secretion, and it is part of the endocrine system, synthesizes a number of hormones necessary to maintain homeostasis of the body.

The thyroid gland is a symmetrical organ, consisting of two lobes and an isthmus. The right and left lobes are adjacent directly to the

trachea, the isthmus is located on the anterior surface of the trachea. Some authors separately allocate in a thyroid gland a pyramidal share. In the normal (euthyroid) state, the mass of the thyroid gland is from 20 to 65 g, and the size of the lobes depends on the sex and age characteristics and can vary widely enough. During puberty, there is an increase in the size and weight of the thyroid gland, and in old age, respectively, it decreases. In women during pregnancy, there is also a temporary increase in the size of the thyroid gland, which independently, without

treatment, takes place within 6-12 months after birth.

The thyroid gland synthesizes two iodine-containing hormones-thyroxine (T4) and triiodothyronine (T3), and one peptide hormone — calcitonin. In the tissue of the

thyroid gland, the accumulation of the amino acid tyrosine occurs, which is deposited and stored in the form of a protein-thyroglobulin (a building material for the synthesis of thyroid hormones). In the presence of molecular iodine and the inclusion of the enzyme thyroid peroxidase (TPO), the synthesis of hormones T3 and T4 occurs. Thyroxine (T4) and triiodothyronine (T3) are synthesized in the apical part of the thyroid epithelium. Calcitonin (thyrocalcitonin) is produced by the parathyroid glands as well as the C-cells of the thyroid.

Thyroid hormones are the main regulators of homeostasis of the human body. With their direct participation, the main metabolic processes occur in tissues and organs, the formation of new cells and their structural differentiation, as well as genetically programmed death of old cells (apoptosis). Another equally important function of thyroid hormones in the body is to maintain constant body temperature and energy production (the so-called calorific effect). Thyroid hormones regulate the body's oxygen consumption by tissues, oxidation processes, and energy production, as well as control the formation and neutralization of free radicals. Throughout life, thyroid-stimulating hormones affect the mental, mental and physical development of the body. Deficiency of hormones at an early age leads to growth retardation, can cause bone diseases, and their deficiency during pregnancy-significantly increases the risk of cretinism of the unborn child due to underdevelopment of the brain in the prenatal period. Thyroid hormones are also responsible for the normal functioning of the immune system — they stimulate the cells of the immune system, the so-called T-cells, with which the body fights infection.

According to the world Health Organization (who) among endocrine disorders, thyroid diseases occupy the second place after diabetes. More than 665 million people in the world have an endemic goiter or suffer from other thyroid pathologies; 1.5 billion people face the risk of iodine deficiency diseases. At the same time, according to statistics, the increase in the number of thyroid diseases in the world is 5% per year.

According to various data, from 15 to 40% of the population of Russia suffer from thyroid pathologies, while in some regions, the percentage of patients in need of thyroid treatment is close to 95%. Statistics show that every second person living in Moscow and the Moscow region has a violation of the function or structure of the thyroid gland.

Among the possible causes of thyroid pathologies can be primarily identified poor environmental conditions, lack of iodine and other nutrients in the diet, as well as increasingly common genetic disorders.

Features of the influence of the thyroid gland on the oral cavity

Morphological and functional changes in the thyroid gland affect the general state of the human body, including tissues of the oral cavity, and these impairments usually manifest by early loss of teeth due to caries and periodontal diseases (Evstratenko *et al.*, 2018; Mazzeo *et al.*, 2013; Voloshina *et al.*, 2018). Oral manifestations of thyrotoxicosis include increased susceptibility to caries, periodontal disease, enlargement of extraglandular thyroid tissue, maxillary or mandibular osteoporosis, accelerated teething, and burning mouth syndrome.

Burning mouth syndrome, a condition that causes burning pain in the mouth, and Sjogren's syndrome, a condition that causes dry mouth, are more common in people with thyroid disease.

Patients who have thyroid disease present a problem for dental treatment. Awareness of the status and current stage of treatment is important to understand the possible changes required for dental treatment. The duration of therapy and the current status are important for understanding the metabolic control of patients. The main complications in patients with hyperthyroidism and hypothyroidism are associated with concomitant heart disease (Silva *et al.*, 2019; Dukić *et al.*, 2013; Vehkalahti *et al.*, 1996).

Dentists are required to be aware of the various aspects of the treatment of the disease that can affect the patient.

In turn, the problem of the relationship between oral tissues and materials used for manufacturing of removable orthopedic structures is one of the main in clinical orthopedic dentistry (Girardin *et al.*, 2019; Timoshin *et al.*, 2018, 2019; Sevbitov *et al.*, 2018). Acrylic dental materials are widely used for the manufacture of removable complete or partial dentures. (Timoshin, Sevbitov, *et al.* 2018).

Acrylic plastics in dentistry - as a method of treatment of dental diseases that have arisen on the background of thyroid diseases

A new page in the history of dentistry began in 1935 when the acrylic polymers are beginning to be introduced into dental practice.

Today, acrylic polymers are the main material for the manufacture of medical prostheses around the world.

Currently, dental polymers are 80% of all medical polymers and are represented primarily by polymers and copolymers of alkyl methacrylates.

Commodity form of basic materials is a set of powder-liquid (Kolodkina *et al.*, 2018; Vereshchagina *et al.*, 2004; Gerasimov *et al.*, 1993; Gozha *et al.*, 2010).

The powder may contain the following components a suspension polymer or a methacrylic acid-based copolymer with a General formula.

$\text{CH}_2=\text{C}(\text{CH}_3)\text{-COOR}$, where R- hydrocarbon radical; initiator; dye; stabilizer; turbid. The liquid is a solution in a monomer (methyl methacrylate - MMA) of target additives. When mixing separately stored powder with liquid, a molding mass is formed, which, depending on the composition of the powder and liquid, is cured (polymerized) by heating or spontaneously. After curing, the monomer forms a matrix of the curing product (polymerizate), in which the polymer – powder balls are distributed. The cured polymer-monomer mixture has a heterogeneous structure, which is due to the presence of "old" and "new" polymer in the polymer.

Dental prostheses in the oral cavity are affected by a complex of factors: physical, chemical, biological in an aggressive chemical environment, which is saliva. They are subjected to strong mechanical pressure when processing food. In turn, the material from which the prosthesis is made, directly affects the environment of the oral cavity, its mucous membrane, the body as a whole. Interaction of high-molecular compounds with the human body is a complex multifactorial process (Saxena *et al.*, 2019)

In this regard, the materials used in prosthetic dentistry must meet the following medical and technical requirements:

- sufficient strength to ensure the integrity of the prosthesis;

- the necessary elasticity, eliminating deformation under the influence of chewing forces;
- high impact resistance;
- low density;
- sufficient thermal conductivity;
- high wear resistance;
- indifference to the action of saliva and various food additives;
- lack of adsorption capacity to nutrients and the microflora of the oral cavity;
- a good imitation of natural color and color fastness;
- harmless to the tissues of the oral cavity and the body as a whole.

However, not yet found such materials that are fully would meet all the requirements. Synthetic acrylic plastics have many necessary qualities, including those that put polyacrylates out of competition with other plastics as construction materials for medicine: low water absorptiveness mechanical strength chemical inertness high manufacturability and low cost (Rech-Ortega *et al.*, 2019)

But the use of acrylic polymers has significant drawbacks.

It should be noted that studies relating to pathology the mucous membrane of the oral cavity in using removable plate prostheses are given considerable attention in both domestic and foreign literature.

Researchers dealing with this rather complex problem, different opinions are expressed about the etiology of these phenomena and the required methods of treatment. According to some authors, pathological reactions of the oral mucosa occur due to irritation of nerve elements at different levels of the reflex chain of the autonomic Central nervous system.

In the occurrence of prosthetic stomatitis, certain value it is attached to microorganisms, and the amount of microflora is greatly influenced by the microrelief of the surface of the plate prosthesis the presence of micro-steps, porosity.

The accumulated data to date allow us to conclude that most likely any removable prosthesis is a complex stimulus of mechanical, chemical, chemical-toxic, thermally insulating and sensitizing nature. Although in each case, a single pathogenic factor may be decisive. And

depending on the influence of which of the pathogenic factors is considered by researchers, certain methods of influence on the polymer dentures are used.

Etiology of allergic stomatitis in such conditions has not yet been clearly established, but most likely, it is related to immune response to irritating substance (Zholudev *et al.*, 2004, 2005). Some authors suggest that stomatitis is a sign of intolerance to acrylic plastics occurring in cases where, for unexplained reasons, the human immune system reacts to the appearance of molecules that it cannot recognize (Kasatkina *et al.*, 2010; Kalyvradzhiyan *et al.*, 2010; Lepilin *et al.*, 2003; Nartikova *et al.*, 1977). It is known that in patients with symptoms of endocrinopathy, phenomena of intolerance occur 20% more often than in people who do not have such pathologies. This fact is caused by general metabolism disorder, increased sensitivity and weak immune response (Paschina *et al.*, 1968; Kuznetsova *et al.*, 2018; Platonova *et al.*, 2018;).

According to some authors, the problem of intolerance to acrylates in patients, in particular, suffering from hyperfunction of the thyroid gland, should be solved with the help of complex drug therapy to increase resistance and reduce the level of sensitization of the body (Sevbitov *et al.*, 1999, 2004; Mamedov *et al.*, 2019; Yumashev *et al.*, Semenycheva *et al.*, 2019, Yumashev *et al.*, 2019).

Drug "Endonorm". History of creation.

"Endonorm", is a mixture of dry vegetable extracts of white cinquefoil, prepared according to special technology, the main active component of the product is Albinin.

Extract of the root of white Lapchatki, standardized substance Albinin, is the main active component of the drug, and other components are enhancing and modulating the effect of the first.

Each capsule contains Lapchatka white root extract 200 mg, grass extract succession 80 mg, kelp powder 70 mg, licorice root extract 50 mg.

Due to the biochemical characteristics of each of the components, the effect of their mutual strengthening in the treatment of diseases of the thyroid gland is created.

Studies have shown that the presence of a sum of phenolic compounds in the white Retina

(*Potentilla alba* L.) affects the production of the anterior pituitary thyroid-stimulating hormone, contributes to the normalization of the morphological structure of thyroid tissue and the return of the thyroid gland to the euteroid state.

Licorice naked (*Glycyrrhiza glabra* L.) due to glycyrrhizic acids normalize the adrenal glands, immune, and reproductive systems restore hormonal imbalance of the body.

Polyphenolic compounds contained in a Series of three-part (*Bidens tripartita* L.) have immunomodulatory activity, allow to achieve a maximum therapeutic effect in diffuse toxic goiter and autoimmune thyroiditis.

Laminaria saccharina (*Laminaria saccharina* L.) due to the presence of a wide range of macro - and microelements normalizes biochemical processes in the tissues of the thyroid gland.

Cinquefoil white is quite well known in the folk medicine of Russia and European countries. Its dosage forms are recommended in the complex treatment of various diseases, including the elimination of such disorders of the thyroid gland as: hypothyroidism (hypofunction), hyperthyroidism (hyperfunction, thyrotoxicosis, Graves 'disease-graves'), autoimmune thyroiditis (Hashimoto's thyroiditis), euthyroid goiter (diffuse, nodular/multi-nodular), hyperplasia of the thyroid gland.

Albinin, contained in the white Lapchatke (*Potentilla alba* L.), affects the production of the anterior pituitary thyroid-stimulating hormone, normalizes the morphological structure of thyroid tissue, returns the thyroid gland to the euthyroid state.

"Endonorm" is recommended as a dietary Supplement-a source of glycyrrhizic acid and tannins, an additional source of iodine.

Figure 1. *Lapchatka white*.

Lat. Name - *Potentilla alba* Linnaeus;
Department-Magnoliophyta; Class-
Magnoliopsida; Order-Rosales; Family-
Rosaceae; Genus-Potentilla; Species-alba L.

Lapchatka white is a modest, perennial, and low herbaceous medicinal plant, with a branched rhizome and a height of no more than 30 centimeters, which ends with a rosette of palmately dissected leaves into 5 leaflets. The white color of the petals indicates cross-pollination by nocturnal insects. Blooms in April-June, fruits in June-July. Fruits are dry ovoid, hairy at the base, achenes. Seeds are spread by insects and birds.

On the territory of the Russian Federation grows mainly in the southern regions of the European part to the Urals. Prefers light, especially oak and pine forests, copses, edges and meadows, grassy slopes, and shrubs. Thickets almost do not form. On 1 m² there are no more than 2-3 plants. It is listed in the regional Red books, in particular, in the Red book of Moscow, Smolensk, Ryazan, Lipetsk, and other regions. It is also listed in the Red book of the Republic of Belarus (resolution of the Ministry of natural resources of Belarus No. 14 of 09.06.2004).

Raw material base Lapchatki white insignificant, because insufficiently studied methods of introduction of plants in culture. That is why it is extremely difficult to find a real and properly harvested root of lapchatki white. For the same reason, officially buy in pharmacies rhizomes and roots Lapchatki white can not. There are experimental plots of several hundred square meters (vegetative method of reproduction is used — by dividing the root), the largest of which is located in the Bryansk region (Bryansk region, Unechsky district, D. Sands, SHPP "Ginseng").

Lapchatka white grows in nature very slowly - from seed to adult plants with a rhizome length of 20-30 centimeters takes 10-15 years. Seeds have low germination, and germination time is stretched, seedlings develop slowly. On the rhizome of adult Lapchatki white there are many dormant buds, thanks to which, with the help of vegetative reproduction from cuttings 1-1.5 cm long, you can grow a whole plant. From one rhizome, you can get a few dozen cuttings. Cuttings are planted in spring or autumn. After 4-5 years after painstaking care of cuttings grow

plants suitable for subsequent planting. By this time, the underground part (rhizome and storing roots) also reaches the optimal weight. In the future, the rate of development of the plant is significantly reduced.

For the treatment of diseases of the thyroid gland in folk medicine, raw Lapchatki white began to be used since the XVIII century. At the same time, the underground part is used as raw material — rhizomes and roots, which are harvested in the autumn, after the death of the above-ground mass. It should be noted that the grass Lapchatki white does not have thyroid-stimulating activity. The plant becomes suitable for preparation of medicinal raw materials for the 3-4 year of vegetation. In folk medicine, a decoction of the herb Lapchatki white is used to treat uterine prolapse. Lapchatka white also shows antibacterial activity, so it is used for colitis, enterocolitis, dysentery and other gastrointestinal diseases. Five are used for the prevention and treatment of diseases of the liver, the gastrointestinal tract, in particular, pus. It is used as a local wound healing agent, for this powder from dry grass is sprinkled with boils, boils, carbuncles, abscesses.

A study of the Lapchatka white.

Stage 1. Beginning. The 1970s.

The first clinical trials of Lapchatka white Were conducted by Ukrainian researchers G. K. Smyk and V. V. Krivenko in the early 1970s on the basis of the Clinical hospital under the Council of Ministers of the USSR, and the results of their studies were published in the "Pharmaceutical journal" [1975]. At this same time, about Lapchatke, a white published several articles (Smyk G. K., Krivenko W. W. 1975; Prikhodko E. I. 1976; Smyk G. K. 1982). Candidate of medical Sciences Prikhodko Elena Ivanovna, who observed patients with thyroid disorders, who were treated with white Lapchatka, stated a good therapeutic effect-up to full recovery.

But, unfortunately, research and experiments with Lapchatka white were suspended due to the lack of raw materials and funding.

Stage 2. From 1983 to 1999.

Russia's first Bloodroot white began to grow Kunitsyn, Vladislav Viktorovich. Since 1983, Kunitsyn began to actively promote and distribute

white Lapchatka. Writing from Kiev Botanical gardens is a plant, he started to practice agricultural techniques of cultivation and breeding adults. He has accumulated a large number of letters and grateful responses from people completely rid of various diseases of the thyroid gland. His numerous appeals to all authorities—from the Minister of health of the USSR and various research institutes, to the editors of magazines and Newspapers—year after year contributed to the popularization of the medicinal properties of the plant among herbalists, phytotherapists and other people associated with folk medicine. During this period, he published many articles about Lapchatka Belaya in various popular publications. Based on his personal experience, Vladislav Viktorovich notes that white Lapchatka is effective in treating the thyroid gland both with its increased and decreased function. In 1999, he met a doctor-phytotherapist, candidate of medical Sciences Kayukova Valentina Anatolyevna.

In LLC SHPP, "Ginseng" were planted the first few roots of Lapchatki white and started its industrial cultivation.

Stage 3.

In 2000, the doctor-phytotherapist Kayukova Valentina Anatolyevna set an extensive experiment to study the medicinal properties of the plant with the open publication of medical histories in the newspaper "Green Doctor". Over the course of several years of painstaking work, she managed to observe more than 500 patients in total. Valentina Anatolyevna initiated a new wave of clinical studies of Lapchatka Belaya (after more than 20 years) and did a great job of analyzing the accumulated material. Until now, this work has no analogues and is of interest to readers not only in terms of the results obtained but also the conclusions and recommendations for the use of Lapchatki white for medicinal purposes.

As a result of the research conducted at the research Institute of inorganic chemistry SB RAS (Novosibirsk), the chemical composition of this plant was established. The underground part contains carbohydrates (starch), iridoids, saponins, phenol carboxylic acids, flavonoids (quercetin), tannins (gallotannin) up to 17% (maximum in the flowering phase). The above-ground part contains iridoids, saponins, phenol-carboxylic acids, flavonoids (rutin), tannins (up to 6%). Phenol-carboxylic acids and their derivatives (n-coumaric, ellagic acids), flavonoids

(quercetin, kaempferol, cyanidin) were found in the leaves. Lapchatka is a concentrator Mn, Zn, Cu, Ce, Co, Fe, Si, Al and for Si, Al, Zn, Mn their content exceeds the criterion of the degree of concentration of mineral elements for non-traditional plants in 1.7, 2.5, 3.0, 4.0 times, respectively. It should be noted that white Cinquefoil also contains elemental iodine and anion of iodic acid.

In 2001, Semenova E. F. and Presnyakova E. V. at the I Russian scientific-practical conference "Actual problems of innovation with non-traditional plant resources and the creation of functional products" announced a report on the chemical composition of white Lapchatka and its use for medicinal purposes.

And finally, only in 2005, 40 years later, from the extract of roots and rhizomes of Lapchatki white was isolated active substance-Albinin (Albinin), which has thyroid-stimulating and gonadotropic activity. In particular, this substance is one of the main components of the drug "Endonorm."

Purpose: to study the indicators of trypsin-like activity of mixed saliva in patients with hyperfunction of the thyroid gland, whose dentures were manufactured by standard compression method, and by using proposed therapeutic and prophylactic measures.

2. MATERIALS AND METHODS

For this purpose, examined 34 patients (18 females and 16 males) aged 40 – 60 years with hyperfunction of the thyroid gland. Patients were divided into two groups. The first group (17 subjects) included orthopedic patients, treated with removable prostheses made by traditional compressive method from Ftorax. Orthopedic patients of the second group (17 subjects) received laminar removable dental prostheses with a double-layer basis made using the proposed technique of saturation lamina with "Endonorm".

Individual gaskets in a double-layer basis of a removable denture were made by a direct method using GC "Coe-Soft" dental plastic.

All patients were examined at the baseline

and 2 weeks, 1 and 3 months after orthopedic treatment. Trypsin-like activity (TLA) of mixed saliva was measured by a spectrophotometric method based on a determination of the rate of N-Benzoyl-L-arginine removal from the synthetic N-Benzoyl-L-arginine of ethyl ester substrate (Reanal).

To implement this method, we diluted 0.5 ml of saliva to 2 ml with 0.05 M Tris-HCL buffer (pH 8.0) and, after its pre-incubation, added 1 ml of BAEE solution for 5 minutes. The reaction was carried out in a spectrophotometer thermostated cuvette (at 25 °C). The rate of spontaneous hydrolysis of BAEE was monitored by optical density increase at 253 nm every 5 minutes within 30 minutes interval and compared with a reference sample. The activity was calculated according to Equation 1:

$$TLA = \Delta D_{250}^{30} \times 3 / (1/1 \times 0.5 \times 30) - \Delta D_{250}^{30} \text{ (Eq. 1)}$$

where ΔD_{250}^{30} is the increase of optical density in 1 ml of the sample at 253 nm within 30 minutes;

3 – sample volume (ml);

0.5 – the amount of saliva taken for analysis (ml);

1.1 – the increase in optical density at 253 nm, corresponding to the formation of 1 μmol BAEE in 1 ml of the sample;

30 – reaction time (min).

The results were expressed in micromoles of hydrolyzed substrate per minute per milliliter.

Analysis of obtained results was made by the method of variation statistics using Student's t-test, A p-value <0.05 was considered significant.

3. RESULTS AND DISCUSSION:

Trypsin-like activity (TLA) of mixed saliva in hyperthyroid patients before prosthetics was $47.95 \pm 1.56 \mu\text{mol/ml}$ in the first group and $47.90 \pm 1.55 \mu\text{mol/ml}$ in the second group, where the proposed therapeutic and prophylactic complex is applied (Fig. 2, Table 1).

Figure 2. The trypsin-like activity of mixed saliva after the imposition of laminar removable dentures in orthopedic patients with thyroid hyperfunction ($\mu\text{mol/ml}$)

Table 1. The trypsin-like activity of mixed saliva after the imposition of laminar removable prostheses in orthopedic patients with hyperfunction of the thyroid gland ($\mu\text{mol/ml}$)

Study group	Pre-prosthetics value	Follow-up time		
		2 weeks	1 month	3 months
1 group, n=17	47.95 ± 1.56	56.12 ± 1.72 , p<0.05	55.85 ± 1.68 , p<0.05	55.34 ± 1.49 , p<0.05
2 group, n=17	47.90 ± 1.55	55.94 ± 1.48 , p<0.05	53.65 ± 1.50 , p>0.05	50.22 ± 1.63 , p>0.05

By the second week of follow-up increase of values in both groups was observed: for example, the value of trypsin-like activity in the first group was $56.12 \mu\text{mol/ml}$, in the second group - $55.94 \mu\text{mol/ml}$, that corresponded to a 17% increase comparing to baseline (pre-prosthetics) data. We assume that this reaction was caused by an adaptive response to the presence of a foreign body (removable prosthesis) and did not require any correction of therapeutic measures.

Further monitoring of TLA in mixed saliva showed sufficiently high TLA values in the first group of patients ($55.85 \pm 1.68 \mu\text{M/ml}$), while in the second group we noted stabilization of TLA ($53.65 \pm 1.50 \mu\text{mol/ml}$), p> 0.05.

By the 3rd month in the first group, TLA still remained at a sufficiently high level ($55.34 \pm 1.49 \mu\text{mol/ml}$, p <0.05), but in the second group

evaluated parameter approached baseline value ($p > 0.05$).

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Two weeks after the application of removable dentures, we observed an increase of saliva enzymatic activity in both groups. This phenomenon was considered to be an adaptive response of the patient's body to the presence of removable acrylic prostheses. Further observation (1 month after orthopedic treatment) showed a sufficiently high level of TLA in the first group of patients and normalization of the studied parameters in the second group (received proposed therapeutic and prophylactic complex). TLA value was an indicator of the correctness of the chosen orthopedic and medical tactics; especially it suggested that developed integrated approach based on the use of gasket, saturated with the "Endonorm" was etiopathogenetic. Three months after orthopedic treatment with removable prostheses, the level of TPA in the first group of patients remained sufficiently high, but in the second group it was close to pre-prosthetics values. Obtained results indicate early adaptation and elimination of negative effects of the acrylic basis in hyperthyroid patients of the second group and suggest the need for correction of therapeutic measures in the first group of patients by means of application of the proposed complex.

4. CONCLUSIONS:

It was revealed that after applying

removable laminar prostheses in hyperthyroid orthopedic patients, violation of the enzymatic activity of mixed saliva is observed. In two weeks, trypsin-like activity was 17% higher compared to the baseline value. This fact was considered as the cumulative effect of thyroid dysfunctions and the effects of acrylic plastics.

It has been established that the use of the proposed curative and prophylactic complex based on "Endonorm" and the use of "Coe-Soft" gaskets in patients with thyroid hyperfunction can prevent the development of intolerance to acrylic removable prostheses.

5. ETHICS COMMITTEE:

All research methods under this article have been conducted in accordance with the relevant guidelines and regulations. All experimental protocols were approved by the Local ethics Committee of I. M. Sechenov First Moscow State Medical University (Sechenov University) protocol number № 10-16 or 09.11.2016. Prior to the study, informed consent was obtained from all patients for the upcoming study.

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