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Contents

Article

Hormonal Restructuring in the Body of Women During the Menstrual Cycle in the Context of the Influence on the Vocal Apparatus

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Abstract: Fluctuations in hormones during the menstrual cycle affect the vocal apparatus. During the follicular stage, a woman's voice improves every day until ovulation. After ovulation, with changes in hormonal balance, the vocal apparatus undergoes changes. Impaired vocalization of high notes, lack of breathing, and hoarseness accompany a woman several days before and during menstruation.

Keywords: voice apparatus, menstruation, menstrual cycle, voice disorder, estrogens, progesterone.

1. Introduction

It is well known that the larynx is a hormone-dependent organ. Throughout a person's life it undergoes changes under the influence of thyroid, sex and growth hormones. These changes have their own peculiarities depending on the sex and age of the person and from this point of view more attention is paid to the female vocal apparatus. During the menstrual cycle, with each phase, the female body undergoes significant changes. Especially strongly these changes affect the professionals of the vocal sphere.

2. Aim

To summarise significant changes in the body during the different phases of the menstrual cycle and to assess their contribution to changes in vocal function.

3. Discussion

3.1 Follicular.

Each new cycle begins with menstruation, during which the main visible process is the renewal of the epithelium in the uterus [1]. This is ensured by the coordinated work of the hypothalamus and pituitary gland [1]. The pituitary gland secretes oxytocin in amounts necessary to influence the uterine musculature to renew itself [1]. There is also the release of vasopressin, which increases blood pressure and affects the distal renal tubules, which leads to water retention, changes in vascular permeability favours the release of the liquid component of blood into the intercellular space [1-3]. The result of these processes, among other things, is oedema of laryngeal structures.

During the follicular phase, as ovulation approaches, estrogens gain their activity and quantity [2]. Estradiol (E2) as its most active form during the most active years of a woman's life [2].

E2 interacts in the body with estrogen receptors (ER-alpha and ER-betta) [2]. It is formed from androgens and is a kind of anabolic. There are receptors for estrogen on blood vessels, muscles, nervous tissue, bones, secretory cells [4]. The effects of estrogen in the body besides those related to the regulation of sexual functions are quite diverse [4]. Estrogen receptors have been proven to be present in skeletal muscles and heart muscles [2-4]. Estrogens have a significant effect on mitochondria [3]. The interaction between estrogen and mitochondrial receptors ensures

regulation of their function, vascular, muscle and neuronal defence, modulation of ATP and AFC production, antioxidant defence, and calcium metabolism [4, 7].

There are 2 lines of action [3]. It is not for nothing that estrogens are called defenders of the organism, they prevent bone resorption, have an anabolic effect, maintain the integrity of the extacellular matrix, participate in collagen metabolism [4, 6]. In addition, they support cardiac vessels due to the activation of NO-synthetase and prevent the development of CHD [5]. Exchange of water, nitrogen, salts in the body, to maintain an optimal balance [3-5]. All these effects and interactions maximise quality voice in the days before ovulation [13]. Optimal fluid balance ensures adequate hydration and fullness of the vocal folds [4, 13]. Keeping calcium and other elements in balance promotes well-adjusted muscle function currently [2-4, 13].

Also, estrogens increase the expression of progesterone receptors, so that it becomes active after ovulation (Fig. 1) [4].

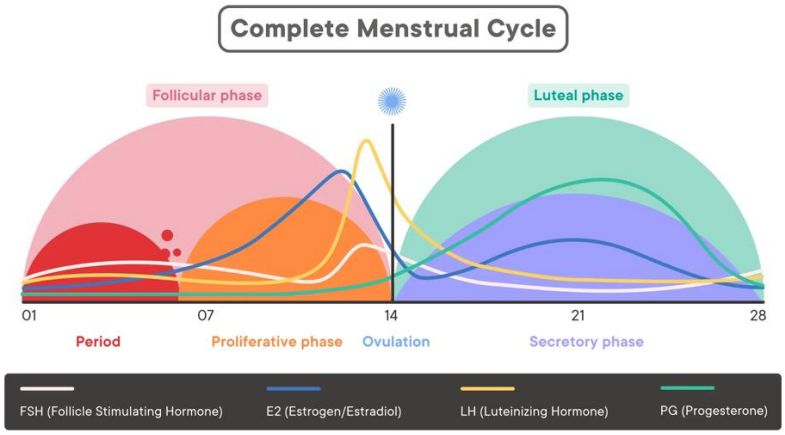

Figure 1. Phases of the menstrual cycle with a schematic indication of the amount of hormones (Source of borrowing - resources of the World Wide Web - https://helloclue.com/articles/cycle-a-z/the-menstrual-cycle-more-than-just-the-period)

3.2 Luteal.

Progesterone belongs to the group of progestagens, steroid hormones [2]. Its main mass is synthesised by the corpus luteum, which is formed after the ovum is released. Also, this hormone is synthesised by the placenta, during pregnancy [2, 3].

Its receptors are also scattered throughout the body [8]. It is important to evaluate its effects on the nervous system. Progesterone acts as an inhibitor of central nervous system activity by interacting with nuclear and membrane receptors, and its metabolites bind to neurotansmitter and GABA receptors [9]. Therefore, symptoms such as weakness and lethargy may be observed, also, during pregnancy it causes some sedation and in very high doses it induces sleep [10]. Thus, it indirectly affects the processes of voice and speech formation.

Progesterone in normal concentration promotes the excretion of fluid from the body (progesterone blocks the mineralcorticoid receptor) and a decrease in the secretion of mucous glands, which is observed some time before menstruation [3]. This is provided by a decrease in aldosterone activity and natriuresis [11]. The amount of intercellular fluid decreases. But when its amount falls, aldosterone starts to compensate and there is an increase in fluid retention and oedema [4, 11, 13]. Also, progesterone promotes desquamation of vocal fold epithelium [3, 4, 13]. The relaxing effect of progesterone also extends to the muscles, mainly the uterus, this is necessary so that it does not contract, during the phase of the cycle and in pregnancy [12]. There is still controversy in scientific circles about the presence of progesterone receptors [4, 6]. But it is unequivocally accepted that its fluctuations influence vocal folds [3].

It is in the last days before menstruation, when the influence of progesterone is at its maximum that rapid fatigue, inability to sing or difficulty in singing high notes, hoarseness, and lack of breathing begin [2-5]. Also impaired breathing and muscle coordination has been noted in women with painful menstruation. Because of the pain syndrome, the cortical muscles are tense, and spasms of the laryngeal muscles can be observed.

4. Conclusions

It is well known that the menstrual cycle and fluctuations in hormone levels affect vocal function. At the same time, this influence can be both direct and indirect, mediated through the

nervous system, fluid balance, microelements in the body. But despite this, there is still quite little reliable information in the muscles and mucosa of the larynx. In our opinion, this is a great asset of our organism, which should be studied further.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

The article is completely written by artificial intelligence and the authors have checked its content.

The authors are responsible for the content of the article written using artificial intelligence technologies.

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Article

Comparison of Acute Pain Syndrome after Surgical Interventions In the Nasal Cavity and Rhinoplasty

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Abstract: Background. Currently, there are very few studies aimed at assessing acute pain syndrome depending on the type of rhinosurgical intervention, which determines the relevance of this issue.

Objective: to compare the intensity of acute pain syndrome after septoplasty, rhinoplasty and rhinoseptoplasty.

Materials and methods. A total of 98 patients aged 18 to 45 years were examined and operated on. Patients of group 1 underwent rhinoplasty, group 2 underwent rhinoseptoplasty, and patients of group 3 underwent septoplasty.

Anesthetic aid was provided using general anesthesia with 1% propofol emulsion; muscle relaxant – atracurium bezilate solution; fentanyl analgesic. Dexamethasone was used as an anti–inflammatory drug, and ondansetron hydrochloride dihydrate solution was used to prevent vomiting. Infiltration anesthesia with 2% lidocaine solution was used locally during rhinoplasty, and conduction anesthesia of nerves innervating the operative area was also performed. Ketoprofen was used before and after surgery, depending on the severity of the pain syndrome.

Acute pain syndrome was assessed using a visual analog scale (VAS) and a digital rating scale (CRS) 1, 3, 6, 24, 48 hours after surgery.

Results: In group 1, according to the VAS scale, the pain intensity was maximum one hour after rhinoplasty (46.29 ± 3.29 mm) and then had a negative dynamics. In groups 2 and 3, the maximum pain was felt 3 hours after surgery (55.67±1.74 mm and 54.91±2.02 mm, respectively). The results of the pain syndrome assessment on the CRH scale correspond directly to the results on the VAS scale.
Conclusion: Based on the results of the assessment of postoperative pain on all scales, compared with rhinoplasty, septoplasty is a more traumatic surgical intervention, and the combination of surgery (rhinoseptoplasty) in the early postoperative period provokes an increase in the intensity of pain syndrome, compared with septo- and rhinoplasty.

Keywords: septoplasty, rhinoplasty, pain, plastic surgery.

1. Introduction

The elimination of defects in the external nose is one of the most difficult goals in facial reconstructive surgery, which is due to the connection between reconstructive and aesthetic tasks of plastic surgery [1-2]. Simultaneous rhinoplasty and septoplasty complicate these tasks due to the need to restore and/or preserve the internal structures of the nasal cavity, for example, the thickness of the nasal septum in the case of autotransplantation of cartilage, the structure of the external and internal nasal valves, etc. [3, 4]. Currently, there are very few studies aimed at assessing acute pain syndrome depending on the type of rhinosurgical intervention in the available literature, which determines the relevance of studying this issue.

2. Patients and Methods

The study was conducted in the period from 2020 to 2023. 98 patients were examined and operated on, among them 19 men and 79 women aged 18 to 45 years. Group 1 (open rhinoplasty) consisted of 6 men and 27 women (n=33, 18-44 years), group 2 (open rhinoseptoplasty) – 7 men and 26 women (n=33, 20-43 years), and group 3 (septoplasty) – 6 men and 26 women (n=32, 21-45 years old).

2.1. Anesthesiological manual.

The anesthetic benefit was provided using the following means: preoxygenation of 100% O2 5-6 l/min through an anesthetic mask, 20 ml (200 mg) of 1% propofol emulsion; for myoplegia – atracurium bezilate solution (50 mg), intravenously bolus; 2 ml 0.005% fentanyl solution intravenously; intubation of the trachea through the mouth with tubes No. 6.5-8 and subsequent artificial ventilation of the lungs was performed with the Mindray Wato device; sevoflurane 2.5 vol%; 6 ml 0.005% fentanyl solution (0.3 mg); 500.0 ml 0.9% sodium chloride solution, 1000.0 ml Ringer's solution, tranexam 500.0 mg, vetorolac solution (60 mg) were administered intravenously.

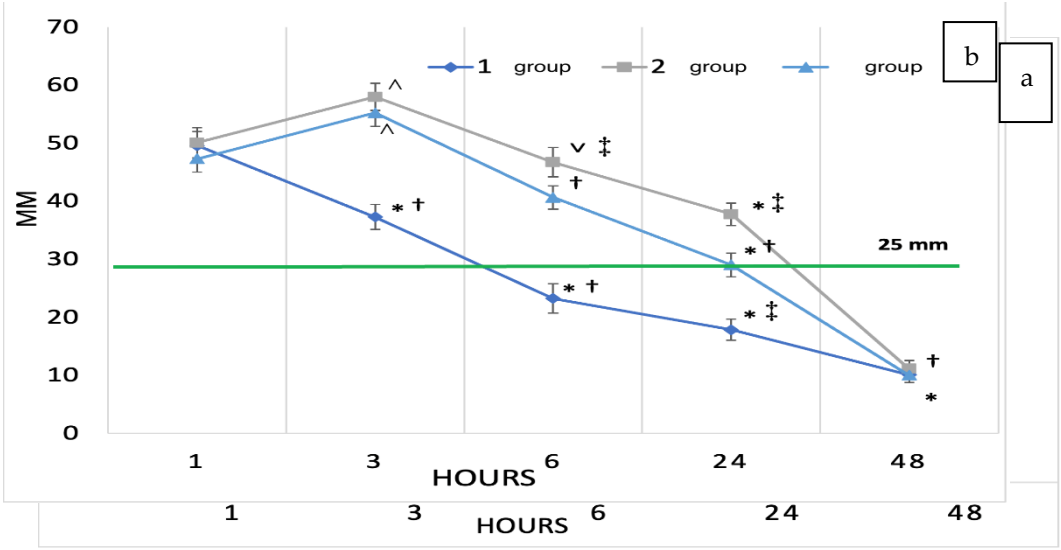
As an anti–inflammatory drug, 2 ml of 0.4% dexamethasone solution at a dose of 0.1 mg / kg, intravenously, bolus, and for the prevention of vomiting - 4 ml of 0.2% solution of ondansetron hydrochloride dihydrate intravenously, bolus.

2.2. Local anesthesia.

During rhinoplasty, infiltration anesthesia was performed with a 2% lidocaine solution in the area of the columella, in the vestibule of the nasal cavity, in the area of the septum, tip, wings, back and root of the nose and lateral slopes, and conduction anesthesia of the subglacial, supra-block and supraorbital nerves was performed. Next, a marginal endonasal and inverted V-shaped transcolumellar incision was performed with a scalpel blade No. 15c. Infiltration anesthesia with 2% lidocaine solution was also performed during septoplasty.

2.3. Analgesic therapy with nonsteroidal anti-inflammatory drugs (NSAIDs).

Ketoprofen solution of 50 mg was administered intramuscularly to all patients as an analgesic before surgery, 24 and 48 hours after surgery and for 3 days after it, depending on the severity of the pain syndrome. Analgesic was used if the pain level on one of the analog pain scales was higher



than 25 mm (Fig.1) [5].

Figure 1. Dynamics of changes in pain syndrome in groups according to the results of its assessment using VAS (a) and CRC (b). Notes: † - significant differences between the timing of pain assessment ($p<0.001$); ‡ - significant differences between the timing of pain assessment ($p<0.01$); ^ – significant differences between the timing of pain assessment ($p<0.05$); * - significant differences between groups after surgery ($p<0.001$); v - significant differences between groups after surgery ($p<0.01$).

2.4. Assessment of pain syndrome.

Acute pain syndrome was assessed using a visual analog scale (VAS) and a digital rating scale (CRH) 1, 3, 6, 24, 48 hours after surgery (Fig.2). Patients were shown scales in the following order and separately: YOURS, CRH. The digital value that corresponded to the pain experienced by the patient met the following criteria: 0 is the absence of pain, and 10 is unbearable, maximum possible pain.

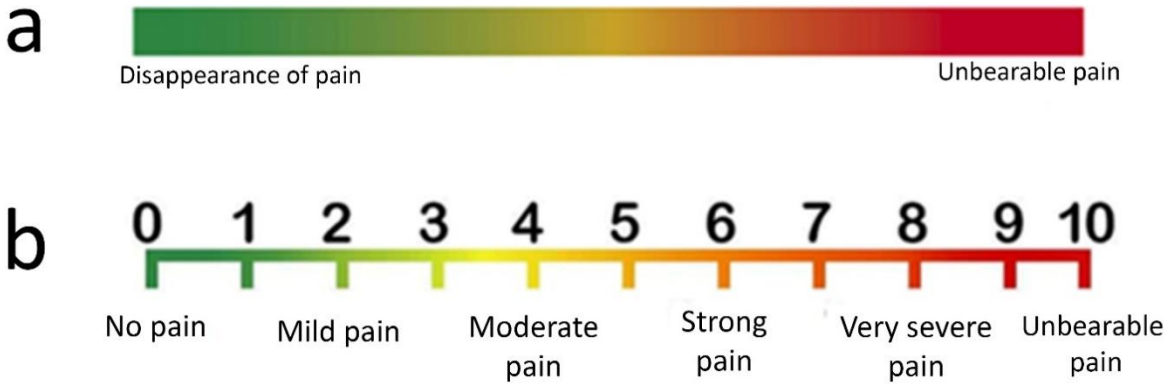


Figure 2. Analog scales for assessing pain. A - visual analogue scale, b - digital evaluation scale.

All patients gave written information consent to surgical interventions and clinical research before performing surgical interventions. The study was approved by the local Ethics Committee of the RUDN Medical Institute, Protocol No. 1 dated 10/21/2021.

3. Results

3.1. Assessment of pain syndrome by VAS.

In the first group, the pain intensity was maximal an hour after rhinoplasty and then had a negative trend: on the 3rd, 6th ($p<0.001$), 24th ($p<0.05$) and 48th ($p<0.001$) hours after surgery. In groups 2 and 3, after 3 hours, according to the Mann-Whitney criterion, the significantly highest pain intensity ($p<0.001$) was recorded, compared with an hour after surgery. In group 2, the pain first and continued to decrease by the 6th ($p<0.001$), 24th ($p<0.01$) and 48th ($p<0.001$) hours after surgery (Fig. 1, Table 1). The same dynamics was recorded in group 3 as in group 2. According to the Mann-Whitney criterion, 3 hours after surgery, patients of group 1 had a significantly lower level of pain syndrome than patients of groups 2 and 3 ($p<0.001$). After 6 hours, the pain syndrome in patients who underwent septoplasty was significantly higher than in patients after rhinoplasty and lower than in patients after rhinoseptoplasty ($p<0.001$) (Fig. 1, Table 1). According to the Student's criterion, 24 hours after surgical interventions in patients of the 3rd group the pain was higher than in group 1 patients ($p<0.01$) and lower than in group 2 patients ($p<0.001$). It should be noted that the pain syndrome at this time of its assessment was higher than the clinically significant indicator of 25 mm only in patients of the 2nd group. Two days after the surgical procedures, the patients experienced almost no pain.

pain assessment time (hours)		1	3	6	24	48
1 group	VAS, mm	46,29±3,29	36,17±2,33	24,62±2,33	19,44±1,73	13,15±1,99
2 group		45,4±2,33	55,67±1,74	48,51±1,84	39,81±1,44	15,33±1,42
3 group		44,36±2,86	54,91±2,02	39,33±1,59	28,67±1,8	16,03±1,41
1 group	NRS, mm	49,59±2,41	37,3±2,13	23,26±2,52	17,87±1,83	10,1±1,33
2 group		50,1±2,62	57,99±2,33	46,72±2,53	37,77±1,95	11,15±1,44
3 group		47,33±2,33	55,212,33±	40,67±1,99	29,05±2,04	10,03±1,21

Table 1. Average indices of pain syndrome in the postoperative period.

3.2. Assessment of pain syndrome according to NRS.

According to the Student's criterion, 3 hours after rhinoplasty in group 1, pain significantly decreased compared to his assessment 1 hour after surgery, and continued to decrease at the 3rd, 6th ($p<0.001$), 24th ($p<0.01$) and 48th hours ($p<0.001$). In the septoplasty group, after 3 hours, the intensity of the pain syndrome significantly increased compared to the previous period of its assessment ($p<0.05$). The same was observed in the same period in the group of patients after rhinoseptoplasty ($p<0.05$) (Fig. 1, Table 1). According to the Mann-Whitney criterion, in group 2, pain syndrome decreased at the 6th and 24th postoperative hours, compared with previous assessment points ($p<0.01$) and continued its negative dynamics on the 48th hour after surgery ($p<0.001$). In the septoplasty group (group 3), the dynamics of pain syndrome intensity was negative ($p<0.001$) (Fig. 1, Table 1). An intergroup comparison of pain syndrome according to the CRH showed that, according to the Student's criterion, 3 hours after surgical interventions, pain was stronger in patients who underwent septoplasty, compared with those who underwent rhinoplasty ($p<0.001$), but lower than those who underwent rhinoseptoplasty ($p<0.05$). According

to the Mann-Whitney criterion, 6 hours after surgery, the pain syndrome in patients of group 1 was significantly lower than in patients of the other groups ($p<0.001$). The intensity of pain in patients after rhinoseptoplasty was significantly higher than after septoplasty ($p<0.05$) (Fig. 1, Table 1). According to the Mann-Whitney criterion, 24 hours after surgery, the intensity of pain after septoplasty was higher than after rhinoplasty, but lower than after rhinoseptoplasty ($p<0.001$) (Fig. 1, Table 1). 48 hours after surgery, patients of all groups, according to the digital rating scale, did not experience pain syndrome and did not differ from each other.

4. Discussion

During rhinoplasty, acute pain syndrome is usually not pronounced, especially with multimodal postoperative analgesia [6-9]. In turn, septoplasty provokes the development of acute pain. So, as it was shown earlier by a number of authors, in conditions of inadequate analgesic therapy, it causes a powerful stress response, manifested both by changes in a number of physiological parameters and the development of pain in the first 3-6 hours [3, 10, 11]. In this study, it was found that patients on all pain scales showed the most severe pain in the rhinoseptoplasty group in the first hours after surgery, which is consistent with literature data [12, 13]. The difference between the rhinoplasty and septoplasty groups can be explained by the difference in the innervation of the external nose and the nasal cavity. Thus, the nasal cavity receives a special vegetative innervation, which ensures the development of stress reactions of the body after septoplasty, which has been shown in clinical [10, 12, 14, 15] and experimental studies [16-21]. Thus, sympathetic nerve fibers depart from T1-T3, form a synapse in the upper cervical ganglia, then pass through the internal carotid plexus and finally join the deep stony nerve and the nerve of the pterygoid canal. The wedge-shaped palatine ganglion in the pterygoid canal also contains sympathetic fibers going to the nose and paranasal sinuses [22].

After rhinosurgery, the severity of pain largely depends on the invasiveness of the operation itself. In most patients, there is a tendency to severe pain for the first time hours after surgery, followed by its decrease over time [12, 23]. The combination of the greatest invasiveness in group 2, compared with the first and third groups, can explain the severity of acute pain syndrome in the postoperative period.

5. Conclusions

Based on the analysis of acute postoperative pain syndrome, this study confirms that septoplasty is a more traumatic surgical intervention compared with rhinoplasty, and the combination of surgery in the area of the external nose and on the nasal septum in the early postoperative period provokes an increase in the intensity of pain syndrome compared with septo- and rhinoplasty.

Application of artificial intelligence: The article is written without the use of artificial intelligence technologies.

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Article

Improving the Provision of Surgical Dental Care in a Polyclinic

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Abstract: Determination of the effect of a gel with natural astaxanthin on the timing of adaptation of the oral mucosa to removable dentures. The gel made from a natural antioxidant reduces the risk of stomatitis, values of hygienic indices and traumatic factor.

Keywords: natural astaxanthin, partially removable denture, hyperemia, anti-inflammatory effect, antioxidant.

1.Introduction

The organization of dental care is important in the field of public health protection as the widest range of medical dental services. The frequency of dental diseases among the population in Russia, as in other countries of the world, ranks first. However, the structure of the organization of dental care in our country does not meet the needs of the population in public and high-quality care.

Purpose of work: To improve the work of the surgical department in the structure of the dental clinic.

2.Materials and methods

The work of two shifts of the dental polyclinic of Moscow was considered. An additional office for acute medical care was introduced in one of the shifts. The efficiency of a shift with an office for acute medical care and a shift without an office for acute medical need was considered.

3.Research results and their discussion

The introduction of an acute medical care office into the structure of a dental polyclinic allowed to distribute the workload of dental surgeons and therapists. The effectiveness of medical work has increased in the shift with the introduction of an acute medical care office, which is proved by the provision of more treatment assistance, as well as tooth extraction. During the shift, the number of completed complex treatment of patients increased during the six months of work of the office for acute medical care.

The provision of medical dental care in Russia has a clear organization, it is provided in specialized dental clinics of cities, dental departments and offices of polyclinics, hospitals and most large general education schools, industrial enterprises, etc. In addition to stationary medical dental institutions, there are mobile dental offices [3]. Dental clinics and schools provide medical

care, where simple medical manipulations are performed. In various institutions, such as hospitals, large multidisciplinary polyclinics, a separate dental appointment is held. In large city hospitals, as well as in military hospitals, assistance is provided for inflammatory, purulent processes, traumatic injuries in the maxillofacial region, including operations on soft tissue neoplasms, where cosmetic surgery is required. In any medical institution, control over the work of all staff is carried out by the chief physician. In each region, city, the work is organized by the chief dentist, who is often the chief physician of the corresponding medical dental institution [4].

Dental care is one of the most widespread types of medical care. The most important tasks of dental organizations are to carry out a complex of dispensary measures for the prevention, early detection, treatment and rehabilitation of patients with diseases of the oral cavity, salivary glands and maxillofacial region.

Medical care for adults with dental diseases is provided in the form of: primary health care; specialized medical care [16].

Dental organizations in which patients receive general and specialized dental care include:

— state and municipal (republican, regional, district, regional, city, district) dental clinics for adults and children;

— educational, research institutes at their clinical bases;

— dental departments and departments of maxillofacial surgery for adults and children as part of multidisciplinary hospitals, medical and sanitary units, departmental institutions, etc.;

— dental offices in dispensaries, women's consultations, centers of general medical (family) practice, health centers of industrial enterprises, educational institutions, etc.;

— private dental organizations (polyclinics, offices, etc.)

The main volume of dental care to the population is provided by dental polyclinics, which are medical and preventive institutions whose activities are aimed at the prevention of dental diseases, timely detection and treatment of patients with diseases of the oral cavity, salivary glands and maxillofacial region.

The most effective is considered to be the provision of dental care to the population according to the precinct principle. The mode of operation of the polyclinic is set by the health authorities according to subordination, considering the needs of the population and specific conditions.

The main tasks of the dental clinic are:

— carrying out measures for the prevention of diseases of the maxillofacial region among the population and in organized groups;

— organization and implementation of measures aimed at early detection of patients with diseases of the maxillofacial region and their timely treatment;

— provision of qualified outpatient dental care to the population.

To solve these problems, the dental clinic carries out:

— provision of timely therapeutic, surgical, orthopedic and other types of dental care to persons who have applied to the polyclinic;

— provision of emergency dental care to patients with acute diseases of the oral cavity, salivary glands and maxillofacial region;

— conducting medical examinations in preschool and school educational institutions, at enterprises with oral cavity sanitation to all those in need;

— dispensary observation of patients with active dental caries, periodontal diseases and oral mucosa, chronic osteomyelitis of the jaws, malignant neoplasms of the face and oral cavity, anomalies of development and deformity of the jaws and other diseases;

— examination of temporary disability of patients, referral to the ITU of persons with signs of permanent disability;

— introduction into practice of modern methods of diagnosis, treatment, new medical equipment, medicines;

— development of territorial targeted programs for the prevention, timely diagnosis and treatment of diseases of the oral cavity, salivary glands and maxillofacial region;

— carrying out sanitary and educational work on the prevention of diseases of the oral cavity, salivary glands and jaws among adults and children [15].

The availability of dental care to the population depends on many factors: organizational forms of its provision, pricing policy, provision of the population with dentists (dentists), etc. Currently, dental care is provided to the population in centralized, decentralized and field organizational forms.

More than 90% of the population begin and finish treatment of dental and oral diseases in outpatient clinics, therefore, the level of medical dental care largely depends on the quality of work. The successful functioning of any medical organization in modern conditions is possible only with the optimal interaction of all departments (links), all elements of the healthcare system [5,7].

The registry plays an important role in the proper organization of admission, regulating the flow of patients by issuing coupons or making an appointment. Primary coupons are issued for an appointment with a dentist-therapist, dentist-surgeon, orthopedic dentist or a specialist of a narrow profile (periodontist, orthodontist, hygienist) [14].

In the organization of the reception of patients in the dental clinic, a major role belongs to the dentist on duty, who examines the patient, determines the type and volume of necessary dental care, directs to other specialists. The dentist on duty provides emergency dental care to patients in emergency cases. Repeated visits to the polyclinic patients are prescribed by the attending physician. With the proper organization of the work of the polyclinic, the patient is observed by one doctor who draws up a treatment plan and, if necessary, directs the patient for consultation and treatment to other specialists [13].

Surgical dentistry is directly connected with other dental specialties — therapeutic, orthopedic, pediatric dentistry and uses common diagnostic and treatment methods with them. This connection is due to the anatomical, topographic and physiological unity of teeth, oral organs, tissues of the maxillofacial region and the pathological processes developing in them.

Diagnostic treatment of dental diseases often consists of consistently performed therapeutic manipulations by methods of therapeutic, surgical and orthopedic dentistry [10].

Primary patients can be admitted to the surgical department both from the registry and from the therapeutic and orthopedic departments; seriously ill and patients with elevated body temperature should be admitted first of all with mandatory registration of the outpatient patient's medical history [11].

If surgical treatment is necessary, the timing, scope and nature of the patient's preoperative preparation are established.

Separately, it is worth noting cases requiring polyclinic dental surgery – removal of retenated, dystopian eighth teeth, operations for the formation of an alveolar process and osteotomy for the possibility of subsequent prosthetics, excision of benign formations of the oral mucosa. This required additional laboratory studies, consultations with specialists of other profiles. Thus, the stage of inclusion and examination of patients showed that the most common reason for contacting a dentist-surgeon are complications of caries and purulent-inflammatory diseases of the jaws. In order to assess the clinical status, an anamnesis was collected with the registration of patient complaints, as well as patient examination data. All information was recorded in a dental chart specially compiled by the World Health Organization in 1997 (Appendix 4). Dental surgical treatment was not started only if there were certain contraindications [7].

On an outpatient basis, only such dental manipulations can be performed, after which the patient can go home alone or accompanied by relatives. The patient's examination data, all manipulations and doctor's appointments, the results of treatment should be noted in the outpatient patient's medical history. The patient's visit is always registered in federal Form No. 37. All medical activities or services are registered in the nomenclature of medical services in healthcare.

The dental range of services is a kind of professional medical services focused on a special benefit - human health. At the same time, in order to maintain, strengthen and restore human health, dentists carry out special interventions, use various invasive and non-invasive methods of influencing organs and tissues of the maxillofacial region.

The provision of high-quality medical dental care is influenced by the number of people who need affordable, free medical care, as well as the number and degree of training of specialists working in medical and preventive institutions [9].

The quality of a dental service is a set of its properties and characteristics related to the ability of the service to meet the needs of the patient in medical dental care. Ensuring the quality of dental care is a very complex problem of organizing a whole complex of administrative, medical and technical measures aimed at achieving and maintaining the normative level of quality [2]. At the same time, the specified regulatory quality level is determined by mandatory standards. In relation to dentistry, a quality standard is a normative document developed on the basis of consensus and approved by an officially recognized body. The quality standard for universal and repeated use establishes rules, general principles or characteristics concerning the provision of medical dental services and (or) its result. One of the factors affecting the quality of dental care is the time of a doctor's appointment per patient. The more time is allocated to one patient, the better the doctor conducts his treatment to the patient [10].

For the population attached to a territorial polyclinic with first-level dental care, a number of advantages are obvious, since it is possible, while visiting doctors of various specialties, to also visit a dentist. The territorial location is of great importance - the bulk of the serviced population are pensioners and disabled people, and the district dental clinic is located at a considerable distance from their place of residence. Institutions of the first level of dental care improve the availability of dental care, including surgical care [11].

In a large medical institution, the dental department works closely with all other departments of the institution. Dental treatment can be carried out in a complex treatment with otorhinolaryngologists, general therapists, endocrinologists and hematologists, surgeons. The therapeutic department itself provides therapeutic, orthopedic, surgical and orthodontic care.

Large dental clinics are divided into adult and children's departments. In turn, the adult is divided into therapeutic, surgical, orthopedic departments. The Children's Department provides therapeutic, orthodontic and surgical care.

The dental department is in close contact with almost all departments of the polyclinic: consultations are held, patients are treated together with doctors: therapist, neurologist, otolaryngologist, endocrinologist, surgeon.

The need for three-level medical dental care of the population in a large city for surgical dental services is important. In the first-level institutions (dental department of the territorial polyclinic), free medical care is provided in the scope of the CHI Program, and more complex types of surgical dental care (including surgical interventions) are provided by the second-level institution (surgical department of the dental polyclinic of the administrative district), both free of charge under the CHI system and on a paid basis [1].

According to Kulikov P.V., most of the patients of the surgical department of the dental polyclinic seek medical help already with complaints of pain (68%), that is, as a rule, with advanced and complicated forms of pathology, which is confirmed by the high level of their caries infestation (on average, 4.1± 0 0.2 carious teeth per person), periodontitis (83.6%) and pulpitis (13.1%). The "burdened" composition of patients in the surgical department of the dental polyclinic is due not only to the insufficient availability of medical care due to its high cost (only 27.7% of patients regularly visit a dentist), but also to the low sanitary culture of those who applied, whose CPI index is on average 18.4 ± 0.4, which means a decompensated state of dental status [12].

At the second level of dental care of the population (surgical department of the district dental polyclinic), secondary and tertiary prevention of diseases of the maxillofacial region is carried out: the number of postoperative complications and hospitalizations in hospitals of the city (departments of maxillofacial surgery, otolaryngological departments, etc.) is less than 1%.

The organization of first-level surgical dental care in dental clinics is advisable in geographically remote neighborhoods from the district dental clinic, which will ensure the availability, first of all, of emergency surgical dental care, as well as dispensary observation of a certain number of patients with chronic dental pathology after surgical interventions or at certain stages of treatment of such patients.

To carry out planned preventive and therapeutic measures in organized groups, the dental clinic uses premises provided for these purposes by the administration of industrial enterprises and other organizations, as well as dental offices (at industrial enterprises with 1,500 employees and above and in higher and secondary educational institutions with 800 students and above) [4].

Most often, a dentist-surgeon is treated with dental problems, as well as complications due to neglect of cases, less often they are treated due to diseases of the oral mucosa and other diseases. Separately, it is worth noting cases requiring outpatient surgery – removal of retenated, dystopian eighth teeth, operations for the formation of an alveolar process and osteotomy for the possibility of subsequent prosthetics, excision of benign formations of the oral mucosa. This requires additional laboratory studies, consultations with specialists of other profiles. Thus, the stage of inclusion and examination of patients showed that the most common reason for contacting a dentist-surgeon are complications of caries and purulent-inflammatory diseases of the jaws. In order to assess the clinical status, an anamnesis was collected with the registration of patient complaints, as well as patient examination data. All information was recorded in a dental chart specially compiled by the World Health Organization in 1997 (Appendix 4). Dental surgical treatment was not started only if there were certain contraindications.

Improving the provision of dental care is an urgent issue today, which was the object of our study.

Materials and methods: In total, 48,615 people applied to the dental clinic in 2021. Of these, 2,497 people were treated for acute pain. In a month, 211 people applied to the polyclinic for acute pain. Of these, 189 people applied to the adult department. The number of people who applied to the polyclinic was registered: for a month, half a year and a year.

The composition of patients of the surgical department of the dental polyclinic was studied by the method of tracing information from official medical documents (medical card of a dental patient - F.№. 043/y;).

The patients of the adult surgical and therapeutic department of the dental polyclinic were distributed with the need for urgent treatment. We compared the number of people who applied in two shifts: without an office for acute dental care and a shift with the introduction of an office for acute dental care. Patients from the registry who applied for acute pain were admitted to the office of acute medical care. The doctor receiving in the office of acute dental care assessed the clinical situation of each patient, conducted an examination. In accordance with the diagnosis, he provided therapeutic treatment for urgent need and referred those patients to whom surgical treatment was indicated for tooth extraction.

The number of patients admitted by doctors in a shift with an introduced acute pain room and the number of patients in a shift without an acute emergency medical care room were

compared (Table 1). Thus, we received information about the state of dental health and the level of sanitary culture of those who applied for medical help, about their opinion about the organization and quality medical care in the appropriate dental institutions.

Table 1. Distribution of patients of the adult surgical and therapeutic department of the dental polyclinic with an urgent need for 2021.

Time period, addresses	The number of people who applied. Shift with an office for acute dental care	The number of people who applied for a shift without an office for acute dental care
Month	118	71
Six months	684	401
Year	1368	687

The number of patients who have applied for acute dental care is shown in Figure 1.

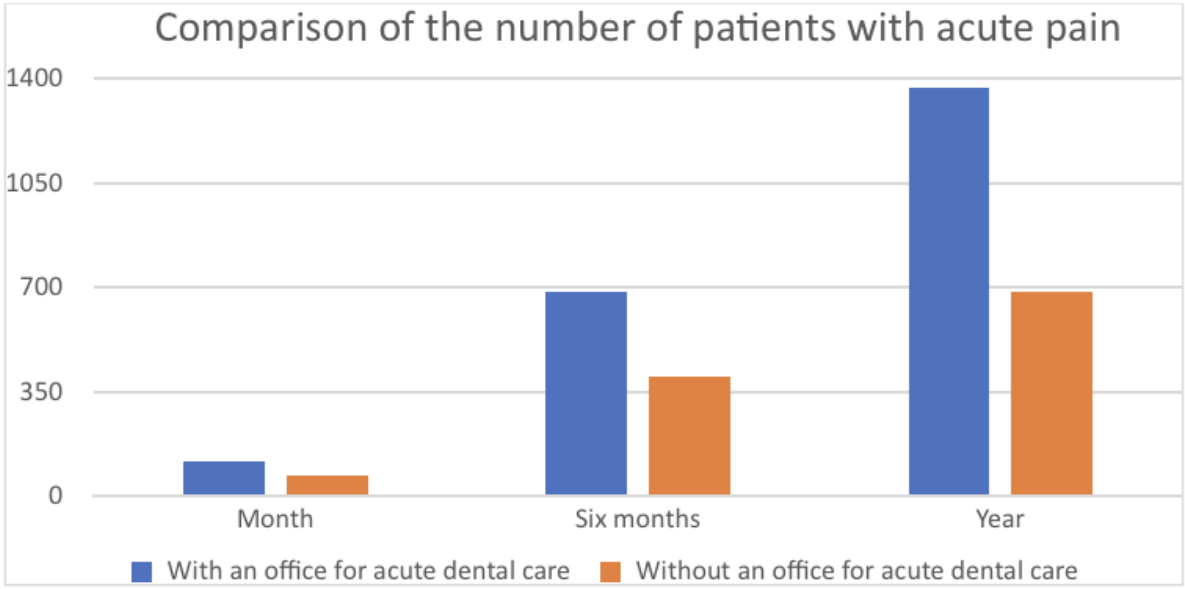

Figure 1. Comparison of patients with acute pain in a shift with an acute medical care office and a shift without an acute medical care office.

The total number of patients who applied for acute pain was 2,497 people.
The number of patients who applied to the adult therapeutic and surgical department was:
189 people per month (February);
1085 in six months;
2055 people for 2021.
The calculation of the number of patients who applied in a shift with an acute pain office and in a shift without an acute medical care office was carried out according to the formula:
Six months:
(118+114+99+126)/4*6=684
1085-684=401

Year:
(118+114+99+126)/*12=1368
2055-1368=687

To calculate the average number of patients who applied to a shift with an acute dental care office for 1 month, statistical indicators for 4 months were taken as a basis – one from each quarter:

February – 118 patients
May – 114 patients
August – 99 patients
November – 126 patients

With these data, the average number of patients per month was calculated using the formula: (118+114+99+126)/4=114,25 (round it up to 114).

Then it was calculated:

The number of patients who applied for a shift with an acute pain office for six months: (118+114+99+126)/4*6=684;

The number of patients who applied for a shift without an office for acute pain for six months: 1085-684=401;

The number of patients who applied for a shift with an acute pain office per year: (118+114+99+126)/*12=1368;

The number of patients who applied to the shift without an office for acute pain for the year: 2055-1368=687.

In the course of the study, the following results were obtained.

4. Research results:

Thus, we received information about the state of dental health and the level of sanitary culture of those who applied for medical help, about their opinion about the organization and quality of medical care in the relevant dental institutions.

The number of patients admitted in 2021 at Dental polyclinic No. 66 for 2021 for the provision of surgical and therapeutic care by dental surgeons and dental therapists was compared (Table 2). The number of patients admitted in both shifts at surgical and therapeutic appointments for a month, for six months and for a year was considered (Figure 2 and figure 3.).

Table 2. Distribution of the number of patients of the adult surgical and therapeutic department of the dental polyclinic admitted in 2021.

Time interval	Therapeutic Department		Surgical Department	
	I shift without an office for acute dental care	II shift with an office for acute dental care	I shift without an office for acute dental care	II shift with an office for acute dental care
Month	588	684	260	282
Six months	3187	3733	1285	1423
Year	6591	7667	2496	2789

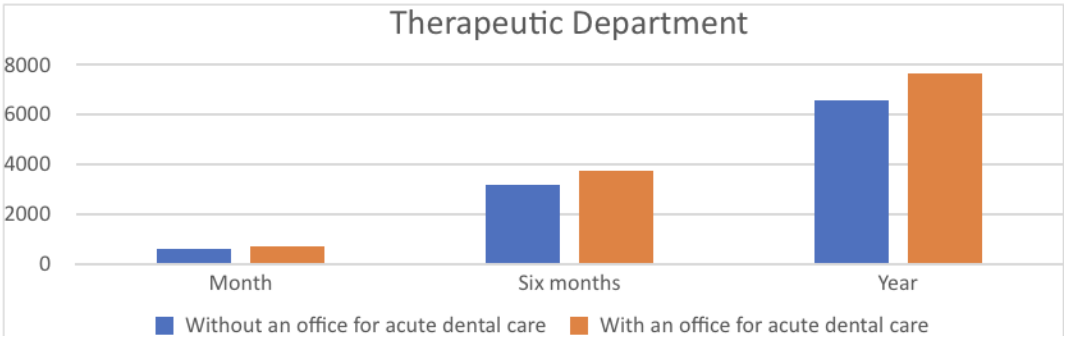

Figure 2. Distribution of the number of patients of the therapeutic department in a shift with an office for acute dental care and without an office for acute dental care.

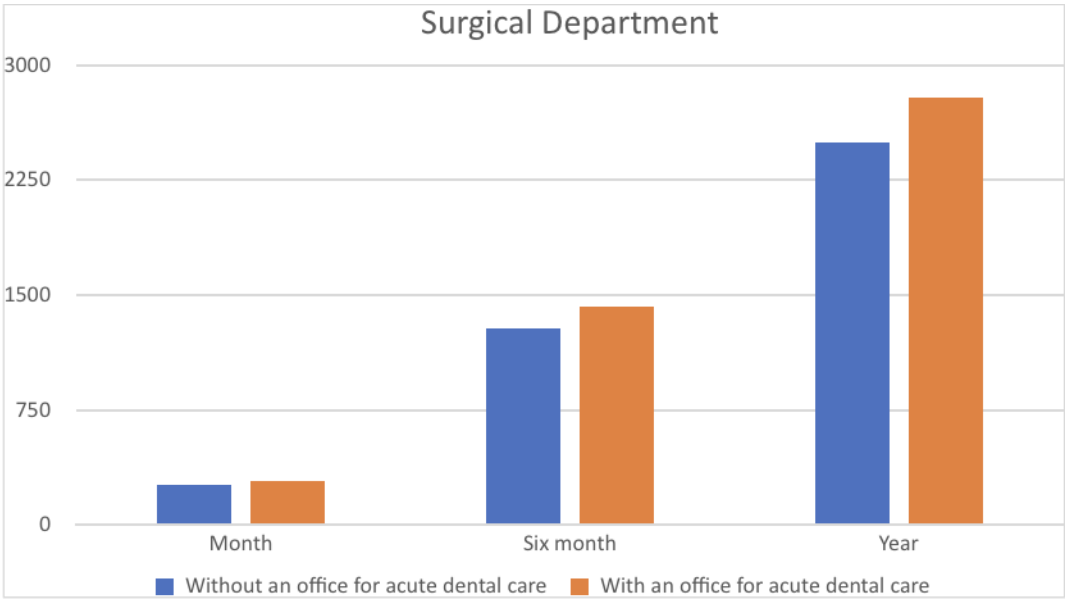

Figure 3. Distribution of the number of surgical department patients in a shift with an acute dental care office and without an acute dental care office.

Thanks to the introduction of the office for acute acute medical care, it allows the number of patients to be received by dentists, therapists and surgeons less and more qualitatively. The number of completed complex treatment for 2021 of work in shifts with an acute medical care office and shifts without an acute medical care office was calculated (Table 3).

Table 3. Distribution of patients with completed complex treatment of the adult surgical and therapeutic department of the dental polyclinic accepted for 2021.

Time period, addresses	The number of patients who applied for a shift with an acute dental care office	The number of patients who applied for a shift without an office for acute dental care
Month	243	128
Six months	1292	727

Year	2749	1412

The efficiency of dental surgeons and dental therapists is higher in a shift with an acute medical care office compared to another shift.

The number of patients with completed complex treatment of the adult department of the dental polyclinic with an office for acute medical care was more by 1,337 people (Figure 4) than the number of patients per shift without an office for acute medical need in 2021.

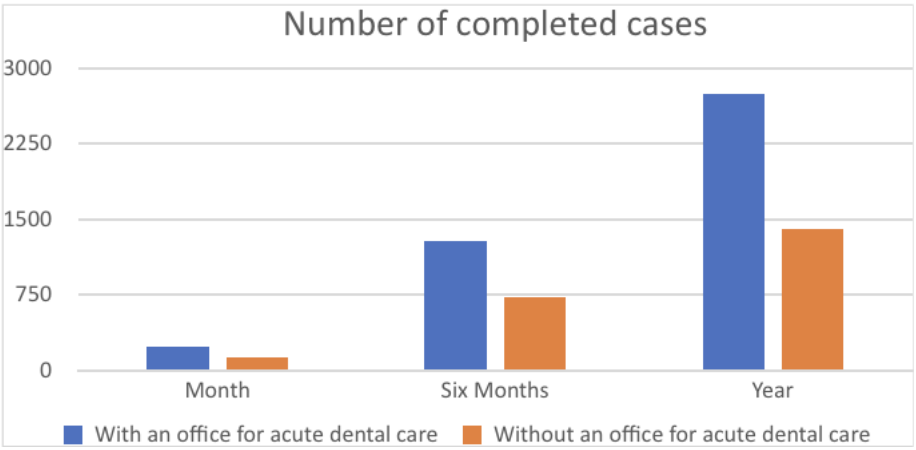

Figure 4. The difference in the number of patients with completed treatment shifts with an office for acute dental care and shifts without an office for acute dental care.

5. Conclusion

In conclusion, we can say that the provision of sufficient scale and range of dental services should be combined with the proper volume and level of quality. The correct distribution of patients affects the effectiveness of doctors. The office of acute medical care allows you to receive a larger number of patients and perform a larger amount of medical work, which directly affects the amount of completed complex treatment.

1. The office for acute medical care allows you to unload dentists-surgeons and dentists - therapists.
2. The number of patients admitted to a shift with an acute medical care office was 1369 more than patients admitted to a shift without an acute pain office.
3. In 2021, the number of patients with completed treatment amounted to 2,749, which exceeded the number of patients per shift without an office for acute pain by 1.95 times.

Application of artificial intelligence: The article is written without the use of artificial intelligence technologies.

Conflicts of Interest: The authors declare no conflict of interest

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Article

The Effect of Astaxanthin as the Strongest Antioxidant on the Human Body.

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Abstract: Periodontal is a set of complex complex tissues that hold the tooth. If the violation adequate oral hygiene in inflammation, in which the antioxidant defense system of the person is not coping According to the synthesis report of the who (1978), chronic gingivitis in the European population is found in almost 80 % of children 10-12 years old and up to 100 % of children aged 14 years. Traditional methods of treatment aimed at eliminating the microbial factor are not always effective enough. Thus, periodontal diseases are an urgent problem today. Of great interest is the natural Astaxanthin, which surpasses other antioxidants in its anti-inflammatory and immunomodulatory properties.

Keywords: periodontal disease, antioxidant, astaxanthin, peroxidation, beta-carotene, Hematococcus pluvialis.

1.Introduction

Inflammatory diseases of periodontal tissues play a leading role in the structure of dental morbidity in Russia [4]. Their early signs are revealed in the form of bleeding gums and tartar [1]. Tissue hypoxia and an increase in the activity of free radical oxidation play a key role in the pathogenesis of many inflammatory diseases of the periodontal mucosa, which leads to the intensification of lipid peroxidation, the release of enzymes and inflammatory mediators with pro-oxidant action [8].

2. Purpose of work

Improving the treatment and prevention of patients with inflammatory periodontal diseases with a new therapeutic and prophylactic agent based on astaxanthin. The research task is to develop innovative forms of therapeutic and preventive tool and incorporate it into clinical practice for patients with periodontal disease.

3. Materials and methods

Astaxanthin was studied in the eyes of rats.

4.Research results and their discussion

In the conditions of changing external environment, in response, the body activates protection systems in order to maintain the constancy of its function and structure. There is a multicomponent response aimed at eliminating the imbalance induced by a shift in metabolic equilibrium. If it is impossible to achieve equilibrium in the metabolism, one or another pathology

develops [3]. The leading role of antioxidants is to prevent oxidation processes, preventing the action of free radicals on the cells of living organisms, thereby slowing down the aging process.

A new progressive direction in the treatment of periodontal diseases is the use of antioxidants. It is proved that the oxidative process, which leads to a sharp increase in the number of reactive oxygen species, which are free radicals, causes cell death.

Toxic substances are actively synthesized when the blood supply to tissues slows down, the local immune status decreases, because normally they perform protective functions, damaging the shells of microbes. However, in the presence of various conditions that have a long-term pathological effect on the body, uncontrolled formation of a large number of free radicals occurs, which the body's own antioxidant system cannot cope with.

Antioxidants are various natural products and their components. They protect the body from the inevitable harmful effects of oxygen. Astaxanthin, as a natural antioxidant, is present in various amounts in all living organisms on earth [6]. It is the most powerful antioxidant today [7]. Astaxanthin belongs to the group of carotenoids. Carotenoids are pigments that give some foods a rich bright color. A large amount of astaxanthin is found in algae and plankton, which are the basis of many food chains, so it can be found in the organisms of various animals. For example, red fish, crustaceans. The rich and beautiful color of flamingos also provides astaxanthin. Most of it is contained in the algae Hematococcus pluvialis (Haematococcus Pluvialis).

Many dietary supplements and even food products are considered antioxidants, but only natural astaxanthin prevails over others in its properties.

Here are just some of the properties that other carotenoids do not possess, but are inherent in natural astaxanthin:

1. Overcoming the blood-brain barrier. Supplying the brain and central nervous system with an antioxidant, providing an anti-inflammatory effect.

2. Penetrates into the retina of the eye, providing the eyes with an antioxidant and having an anti-inflammatory effect.

3. It spreads throughout the body, exerting an anti-inflammatory effect on all organs and skin, while simultaneously supplying them with an antioxidant.

4. Penetrates the cell membrane.

5. Interacts with muscle tissues.

6. Acts as the strongest antioxidant, quickly catches free radicals and extinguishes singlet oxygen.

Those companies that used astaxanthin as a dietary supplement in the early 1990s advertised it as the strongest antioxidant, but its other benefits became known much later. People taking these dietary supplements talked about how their well-being improved significantly, arthritic pain disappeared, the number of colds and flu decreased, and also allowed them to stay in the sun for a long time without the risk of getting burned.

Two independent studies have shown that Astaxanthin is the strongest antioxidant [7]. There are several ways to measure the strength of an antioxidant. The most common to date: The ability to absorb oxygen (ORAC), developed in the laboratory of Brunswick, Massachusetts, USA [8]. But according to the laboratory, this experiment is not suitable for oil-soluble carotenoids. Therefore, natural astaxanthin was tested in other ways.

According to the results of one of the experiments, this antioxidant surpassed vitamin E by 550 times in terms of the method of absorption of singlet oxygen. Vitamin E has always been considered a strong antioxidant in its effect on the body and cosmetic effect, but natural astaxanthin surpassed it. A comparison was also made with other antioxidants in terms of the level of singlet oxygen quenching (Fig.1, 2).

A comparison [2] of natural astaxanthin with lutein, beta-carotene and vitamin E in terms of the level of singlet oxygen quenching is presented in Figure 1.

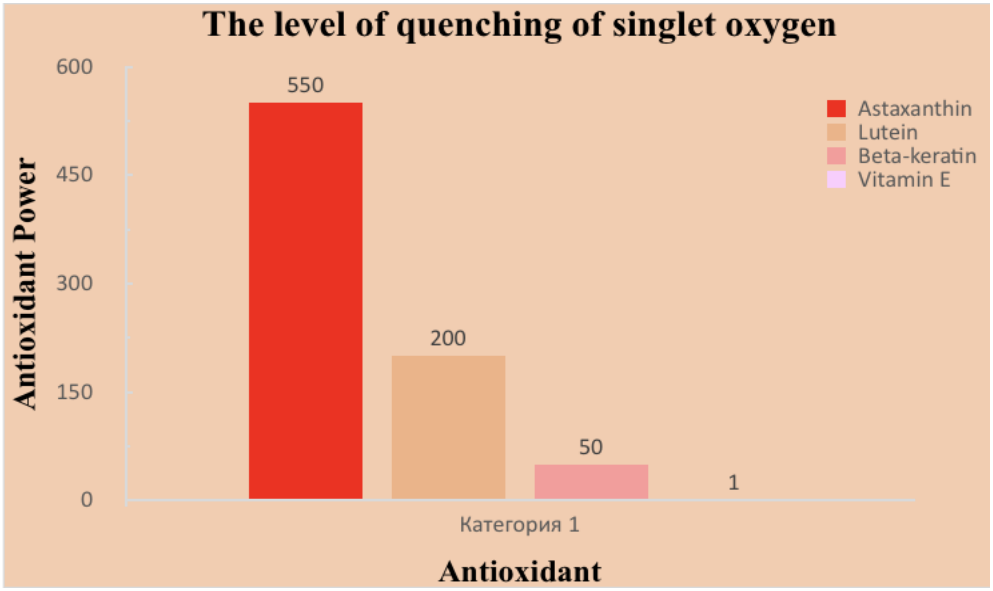

Figure 1. Comparison of Natural Astaxanthin with Lutein, Beta-carotene and vitamin E by the level of singlet oxygen quenching.

The second study was conducted at Creighton University [2] (Figure 2). Scientists compared Natural Astaxanthin, Vitamin E, Vitamin C, Pycnogenol, synthetic Astaxanthin and other antioxidants by the level of destruction of free radicals. Studies have shown that Natural Astaxanthin is 14 to 60 times more powerful than all other antioxidants [2].

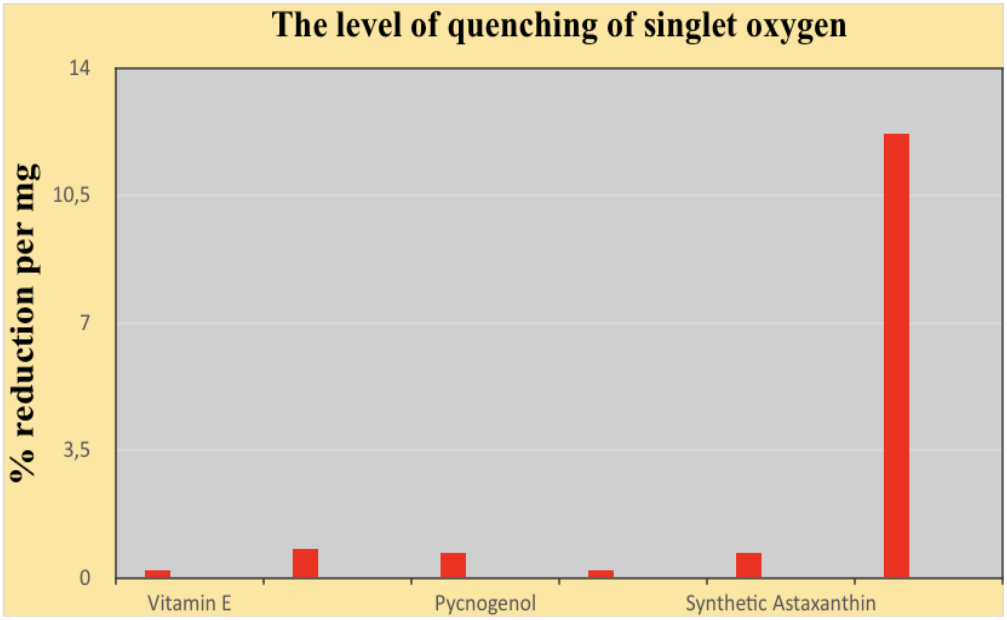

Figure 2. Comparison of Natural Astaxanthin with vitamin E, vitamin C, Pycnogenol, Beta-carotene, Synthetic Astaxanthin by the level of singlet oxygen quenching.

It was noted that different testing methods gave very different results. In the first experiment, Natural Astaxanthin proved to be 550 times stronger than vitamin E, but in the second experiment it surpassed it by 14.3 times. In the future, many studies have been conducted that have shown that Natural Astaxanthin is indeed the most powerful antioxidant.

Many companies obtain Synthetic Astaxanthin from petrochemical raw materials. Despite the similarity of the chemical formula with natural Astaxanthin, its synthetic analogue is another molecule with a different shape. Natural Astaxanthin has hydroxyl groups at the ends of the molecule that trap free radicals.

Some antioxidants turn into pro-oxidants, enhancing the oxidation process and starting to harm the body. Such antioxidants are vitamin C, vitamin E, zinc, beta-carotene, lycopene, zeaxanthin [3].

In the 1990s, a large-scale scientific experiment was conducted to study antioxidants in Finland. Research data has shown that smokers taking dietary supplements with synthetic beta-carotene suffer from lung diseases more often than those who took a placebo. This is due to the fact that the protection of cells by beta-carotene depends on the presence of other antioxidants in the body, especially vitamin C. With vitamin C deficiency, beta-carotene receives destructive energy and turns into a pro-oxidant. If the amount of vitamin C is normal, then this prooxidant turns into an antioxidant.

The peculiarity of the molecular structure of Natural Astaxanthin is that it never turns into a prooxidant and does not cause harm.

5. Conclusion

One of the important properties of natural Astaxanthin is anti-inflammatory. It fights inflammation in various ways that are closely related to its antioxidant capabilities. The mechanism of anti-inflammatory action consists in the suppression of various inflammatory mediators, such as cell necrosis factor (FOC), Prostaglandin E2 (PE-2), Interleukin 1B (IL-1B), nitric oxide (OA), reducing the effect of C-reactive protein [7]. In one of the experiments conducted at the Medical College of Hokkaido University (Japan), under the conditions of chemical experiment, Natural Astaxanthin suppressed nitric oxide, cell death factor and Intraleukin 1B.

A study was also conducted on rats, which showed the anti-inflammatory effect of Astaxanthin on the eyes of rats, suppressing the effect of inflammatory mediators [7].

In addition, antibacterial action has been shown on Helicobacter pylori in patients with gastric ulcer. Helicobacter pylori is a bacterium that settles in the epithelium of the human stomach and causes type B gastritis, gastric ulcer, duodenal ulcer and stomach cancer. After infection, a chain of events occurs on the gastric mucosa, leading to the activation of phagocytes, which leads to damage to the mucous membrane and inflammation. Recent studies have shown that mice infected with H. pylori and then consuming Haematococcus extract, there is a significant decrease in inflammation and the number of bacteria in the stomach. Treatment of infected mice with Haematococcus algae reduced the total number of bacteria by four times, and inflammation by 35%. These positive results are associated with the modulation of the immune response, as well as the neutralization of reactive oxygen species, the appearance of which accompanies inflammation. [5,6]

In a number of other experiments, the protective effect of Astaxanthin on the retina of the eye has been proven. The yellow spot is a small area in the center of the retina, consisting of cones, which are responsible for distinguishing colors. This area provides the clear vision needed to read and to distinguish fine nuances. Photoreceptor cells of the retina contain a large amount of polyunsaturated fatty acids, and are relatively highly saturated with oxygen, which is associated with an increased probability of lipid peroxidation. It is known that high-energy blue light is capable of generating reactive oxygen species in the process of photooxidation, mainly a singlet form capable of generating peroxides and other unstable molecules that can damage lipids. The accumulating oxidative process leads to degenerative changes noticeable in the aging spot. Blue light in the spectral region (400-500 nm) damages the retina, generating unstable forms of oxygen inside the eye. Clinical studies have shown that light burns are the main cause of the disease, the so-called "age-related macular degeneration". Due to its unique ability to cross the blood-brain barrier, astaxanthin can provide protection against oxidation to the retina, brain, spinal cord, and nerves. In the USA, the University of Illinois owns a patent for the use of astaxanthin as a means to combat age-related macular degeneration. The optimal dose of astaxanthin for visual fatigue was determined, which was 6 mg per day [6].

In large doses, Astaxanthin has demonstrated neuroprotective effect, preventing the phenomena of stroke and ischemia. Current studies show that this antioxidant can improve memory in the case of multiinfarction dementia [2].

The results of experiments with ultraviolet irradiation have shown that Natural Astaxanthin is able to complement the antioxidant systems of cells, reducing damage to the DNA structure. It specifically affects transglutaminase enzymes that help neutralize harmful polyamines resulting from skin irradiation [5].

Singlet oxygen is toxic to the immune system due to its ability to catalyze the occurrence of free radicals that can damage blood cells. Prolonged stress caused by intense physical exertion can lead to a violation of the immune system, for example, disrupt the activity of cells such as T-killers

or certain antibodies. Carotenoids strengthen both the specific and non-specific immune system and protect cell membranes and DNA from mutations from destruction, also having a strong stimulating effect on the immune system. Astaxanthin also enhances the secretion of Interleukin-1 alpha and Tumor Necrosis Factor alpha significantly more than astaxanthin or beta-carotene.

In the course of one of the studies, it was shown that astaxanthin had the greatest cytokine-stimulating activity among the tested substances, and that this carotenoid is even able to play the role of an immunomodulator. Studies have shown that the synthesis of immunoglobulin M increases with the intake of astaxanthin even in small concentrations.

The significance of periodontal diseases as a general medical and special problem is determined by their prevalence in the world, a large loss of teeth and the negative influence of foci of infection with the formation of a periodontal pocket. [1]

Periodontal diseases are divided into inflammatory (periodontitis) and dystrophic (periodontal disease). Their causes have not been definitively clarified. For a number of reasons (vitamin and protein deficiency, violation of the intake of trace elements into the body, excessive consumption of carbohydrates and fats with food, smoking, hereditary predisposition, etc.) with periodontitis, the periodontal blood supply deteriorates, local immunity decreases and microorganisms contained in plaque penetrate into the soft and bone tissues of the jaw, foci of inflammation appear. Periodontal disease is much less common and is manifested by dystrophic changes in bone tissue. The causes of this disease are diabetes mellitus, chronic diseases of the digestive system, hereditary predisposition. These causes cause circulatory disorders in the tissues surrounding the tooth. The oxidative process triggers a certain "metabolic cascade", or, in other words, a set of interrelated pathological reactions that irreversibly damage the cell and lead to atrophy of jaw tissues and loss of teeth. One of the main reasons for the development of periodontal diseases is inadequate oral hygiene. Modern dentistry offers the treatment of periodontal diseases with antioxidants, by introducing them into toothpastes. Astaxanthin, which is part of pastes, significantly increases their antimicrobial properties, leads to the restoration of intracellular metabolism and stimulates regeneration processes [6].

Modern innovative biotechnologies of production make it possible to obtain stable astaxanthin that does not break down under the influence of environmental factors. Modern science continues to study the properties of the release of this strong natural antioxidant. In the near future, Natural Astaxanthin will be used more widely. You can only fantasize about where and how its anti-inflammatory properties will be useful.

Application of artificial intelligence: The article is written without the use of artificial intelligence technologies.

Conflicts of Interest: The authors declare no conflict of interest

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Article

The Relevance of the Use of Natural Astaxanthin in the Prevention and Treatment of Inflammatory Periodontal Diseases

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Abstract: Recent studies have shown that the development and occurrence of chronic periodontitis is associated with the state of the human immune system and its ability to adequately respond to microbial antigenic stimulation. In recent years, an increase in inflammatory periodontal diseases has been observed in the developed countries of the world. In this regard, the need for therapeutic and prophylactic agents with immunomodulatory and anti-inflammatory effects is increasing. Currently, the use of natural antioxidants as a therapeutic and prophylactic agent is becoming relevant. The article discusses the properties of natural astaxanthin as one of the most powerful natural antioxidants.

Keywords: astaxanthin, an antioxidant, inflammation, periodontitis.

1. Introduction

Inflammation is a complex, local and general pathological process that occurs in response to damage to the cellular structures of the body to the action of a pathogenic stimulus and manifests itself in reactions aimed at eliminating damage products, and if possible, agents (irritants), as well as leading to maximum recovery in the area of damage under these conditions. With inflammation, all types of metabolism are activated, pH readings decrease to 6.0 and below, osmotic pressure increases, contributing to the swelling of colloids. Inflammatory mediators such as prostaglandins, serotonin, histamine, bradykinin enhance the inflammatory response, which contributes to vasodilation and increased permeability. As a result, the amount of exudate and the level of endogenous pyrogens increases. The barrier function of the lysosome membrane is disrupted, aggressive simple- and hydrolytic enzymes that intensify the inflammatory process enter the cytosol [2].

Inflammatory periodontal diseases occupy the second place in frequency and prevalence among all dental diseases. This pathology covers 65% of the adult population of most developed countries of the world [3]. A sharp increase in the prevalence of periodontal diseases, the loss of a large number of teeth (more than with any other disease of the dental system), a violation of

chewing function and speech, the effect on the general condition of the body (decreased reactivity of the body, microbial sensitization, the development of allergic conditions, etc. D.) and the decline in the quality of human life force us to consider periodontal diseases as a special section in dentistry, and the problem is made not only general medical, but also social.

2. Purpose of work

To study the effect of astaxanthin in the prevention and treatment of inflammatory periodontal diseases.

3. Materials and methods

Conducting research at the Medical College of Hokkaido University (Japan), under the conditions of chemical experiment, natural astaxanthin suppressed nitric oxide, cell necrosis factor and Interleukin 1B.

4. Results and discussions.

In the periodontal tissues of healthy people, there is a balance of anti-inflammatory and anti-inflammatory cytokines that regulate the immune response to microbial infection. In patients with inflammatory periodontal diseases, the total amount of IL-1B, IL-5, IL-6 and IL-8, TNF-α and TGF– and IFN-α is significantly higher than in healthy patients, while the amount of IL-4 had an inverse relationship with periodontal status. It is known that a number of cytokines have powerful anti-inflammatory and catabolic activity, which leads to damage to periodontal tissues. With an extensive intake of microbial agents, mediators go beyond the expediency and become uncontrolled. Cytokines induce epithelium, fibroblasts and macrophages to produce a large number of inflammatory mediators and neutral metalloproteinases, which leads to inhibition of the extracellular matrix and further destruction of bone tissue. A prerequisite for the development of inflammation and an inadequate immune response is the complex interaction of the leading link in the development of this pathology of the microbial factor (bacterial plaque) and periodontal tissues [1].

Thus, a local imbalance of cytokine production at the level of the damaged organ determines the mechanism of development of a chronic inflammatory process in periodontal tissues, which necessitates immunotherapy with drugs that have both corrective and antibacterial effects on the cytokine status in the damaged periodontal [4].

Most of the currently existing antibacterial drugs are products of synthetic origin. They have a high therapeutic effect, however, with prolonged use of such funds, the appearance of resistant strains of microorganisms may occur, leading to a decrease in the effectiveness of treatment and prevention of periodontal diseases. In addition, the range of medicines developed on the basis of domestic medicines is insufficient [5,6].

It would seem that the most effective means of preventing the formation of dental deposits is their mechanical removal from the surface of the teeth using brushes and threads. However, a significant part of the population (30%) is not able to clean their teeth on their own. That is why therapeutic and prophylactic agents require enhanced antimicrobial, immunomodulatory and anti-inflammatory action, without the risk of complications [6].

Modern dentistry offers the treatment of periodontal diseases with antioxidants by introducing them into toothpastes and therapeutic and prophylactic gels and adhesive films. Antioxidants are substances that protect the cells of our body from external and internal toxic effects. Thanks to the antioxidant protection system, the level of tissue damage is reduced, the recovery process is accelerated. The strongest natural antioxidant is astaxanthin. It is superior in power to other natural antioxidants. Astaxanthin belongs to the group of carotenoids. Carotenoids are pigments that give some foods a rich bright color. A significant amount of astaxanthin is found in algae and plankton, which are the basis of many food chains, so it can be found in the organisms of various animals. For example, red fish, crustaceans. The rich and beautiful color of flamingos also provides astaxanthin. Most of it is contained in the algae Hematococcus pluvialis (Haematococcus Pluvialis) [9].

Many dietary supplements and even food products are considered antioxidants, but only natural astaxanthin prevails over others in its properties. Here are just some of the properties that other carotenoids do not possess, but are inherent in natural astaxanthin:

1. Overcoming the blood-brain barrier. Supplying the brain and central nervous system with an antioxidant, providing an anti-inflammatory effect.

2. Penetrates into the retina of the eye, providing the eyes with an antioxidant and having an anti-inflammatory effect.

3. It spreads throughout the body, exerting an anti-inflammatory effect on all organs and skin, while simultaneously supplying them with an antioxidant.

4. Penetrates the cell membrane.

5. Interacts with muscle tissues.

6. Acts as the strongest antioxidant, quickly catches free radicals and extinguishes singlet oxygen.

The peculiarity of the molecular structure of natural astaxanthin is that it never turns into a prooxidant and does not harm the body.

One of the most important properties of natural astaxanthin is its anti-inflammatory effect. It fights inflammation in various ways that are closely related to its antioxidant capabilities. The mechanism of anti-inflammatory activity consists in the suppression of various inflammatory mediators, such as cell death factor (FOC), Prostaglandin E2 (PE-2), Interleukin 1B (IL-1B), nitric oxide (OA), reducing the effect of C-reactive protein [7,9].

Unlike other beta-carotenes and vitamin E, astaxanthin contains two additional groups of oxygen molecules, giving it the ability not only to neutralize free radicals, but to stop destructive chain reactions that cause cell death. Due to its special chemical structure, this antioxidant is one of the unique carotenoids - xanthophils, which are very powerful antioxidants. Studies have shown that natural astaxanthin is 10 times more effective than beta-carotene and 100 times more effective than vitamin E. In addition, astaxanthin not only neutralizes free radicals, but also interacts with vitamins C and E, contributing to their effectiveness. Due to its unique biochemical structure, astaxanthin protects the cell membranes of all organs. Unlike beta-carotene, vitamin C and other antioxidants, which are either inside or outside the bilipid membrane, astaxanthin molecules have the ability to localize inside and outside the bilipid membrane, thereby providing an additional protective function of cells. A study was also conducted on rats, which showed the

anti-inflammatory effect of astaxanthin on the eyes of animals, suppressing the effect of inflammatory mediators [8,9].

The introduction of natural astaxanthin into preventive and therapeutic oral hygiene products has a directed antioxidant effect on the oral mucosa and periodontal tissues, thereby preventing their damage. Due to a powerful natural antioxidant, the antimicrobial properties of preventive hygiene products are significantly increased, as well as the restoration of intracellular metabolism is accelerated. Astaxanthin has a local immunomodulatory, anti-inflammatory and keratoplastic effect.

5. Conclusion.

Therapeutic and prophylactic agents for inflammatory periodontal diseases are becoming an increasingly urgent issue today in dentistry. More and more, funds with a powerful immunomodulatory and anti-inflammatory effect are required without side effects and complications. Modern innovative biotechnologies of production make it possible to obtain stable astaxanthin that does not break down under the influence of environmental factors. Modern science continues to study the properties of the release of this strong natural antioxidant. In the near future, natural astaxanthin will be used more widely.

Application of artificial intelligence: The article is written without the use of artificial intelligence technologies.

Conflicts of Interest: The authors declare no conflict of interest

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Article

Study of Wound Healing and Local Irritant Effects of Antioxidant Prophylactic Gel

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Abstract: The effect of dental gel with astaxanthin and polyprenol on the detection of toxicity and local irritant effect on laboratory animals was evaluated. The local inflammatory reaction, wound healing effect, hematological and biochemical parameters of laboratory animals were studied when using a gel with astaxanthin and polyprenol. When conducting a study on laboratory animals, dental gel with astaxanthin and polyprenol showed wound healing effect, absence of toxicity and local irritant effect. The antioxidant gel with astaxanthin and polyprenol showed wound healing properties, as well as the absence of toxicity and local irritant effects on laboratory animals.

Keywords: astaxanthin, polyprenol, dental gel, toxicity.

1. Introduction

The search for new promising dental products with anti-inflammatory, wound-healing, antibacterial and immunomodulatory effects and at the same time showing minimal side effect is quite an urgent task of modern scientific and practical medicine [6,8,9].

Astaxanthin, which is part of the dental gel under study, belongs to the class of carotenoids by its chemical structure and is a natural antioxidant present in various amounts in living organisms [1,3]. Currently, astaxanthin is successfully used in medical practice [2,10]. One of the main tasks in dental practice is to "place" the effective dose of IFN precisely in the focus of inflammation, thus reducing the dosage and the possibility of developing adverse reactions [4,5]. Polyprenols are obtained from the greens of Siberian fir, they play an important function, acting as

natural bioregulators and occurring in small quantities in various plant tissues [4,20]. Polyprenols interact perfectly with antioxidants, increasing the efficiency of their work [3,7].

The gel sample we made contained natural astaxanthin and polyprenol.

2. Materials and methods

The study of wound healing was carried out on mature rats (males, females) with a course of daily intragastric administration of the studied drug and the comparison drug in dosage form for 1 month at the maximum possible dose / volume, which is 1 month at a dose of 0.02 g (100 mg / kg). Rats are the main standard objects in the study of wound healing and local irritating effects of pharmacological substances. The recommended condition for evaluating the studied drug is the use of standard animals of both sexes in the experiment. [1].

The study of the local irritant effect, peripheral blood parameters, biochemical blood parameters on enzyme activity was carried out on rats of both sexes.

The initial body weight (at the first administration of drugs) is 180-200 g, the spread over the initial mass should not exceed ± 10%. Adjustment of the dose of the drug for administration is carried out a week after the start of the experiment based on the latest results of measuring the body weight of animals.

Conditions for keeping animals: standard conditions of the vivarium, placement in groups in marked cages with regularly replaced bedding, with free access to water and food, in conditions of standardized light and temperature conditions.

Each experimental group consists of 10 individuals. The control group consists of 10 individuals. The choice of doses was carried out according to the already available data on the therapeutic dose and the requirements described in the OESD regulatory documentation No. 407. [7,8].

Rats were kept in polycarbonate cages for rats, type R-1, manufactured by Proflab Group of companies, S= 1025 cm2 in groups of 10 individuals of the same sex, on a litter. The floor area in the holding cage for one animal will be 102.5 cm2 (the minimum allowable area is 77 cm2).

Marking of rats is carried out by applying a color mark on the wool (0.5% gentian violet solution).

Clinically healthy animals are included in the experiment after 14 days of quarantine. Conditions for keeping animals: standard conditions of the vivarium, placement in groups in marked cages with regularly replaced bedding, with free access to water and food, in conditions of standardized light and temperature conditions.

Each experimental group consists of 5 individuals of each sex (males, females). The control group consists of 5 individuals of each sex (males, females).

During the experiment, examinations of the animal's condition are carried out in dynamics according to integral indicators; according to functional indicators of the main organs and systems, including physiological, hematological, biochemical indicators with an assessment of histological changes in organs and tissues; as well as with an assessment of local irritant effects (gastrointestinal tract departments).

Statistical data processing was carried out in the GraphPad Prism 8 program (Software GraphPad Software, USA). After determining the normality of the distribution by the Shapiro-Wilk criterion, in the case of a normal distribution, a t-test was used for pairwise comparison or oneway ANOVA (analysis of variance) with the post-hoc Turkey test for multiple comparison. In the case of an abnormal distribution, the Mann-Whitney criterion was used for pairwise

comparison, and for multiple – the Kraskel-Wallis criterion with the Dunn post-hos test. Single-tail tests and a 95% confidence interval were used for the analysis. The differences were considered statistically significant at $p < 0.05$.

3. Results

Effect on body weight, feed and water intake.

During the experiment, the test animals were observed, changes in body weight were recorded weekly. The dynamics of changes in the weight of rats during 30 days of drug use and 14 days after discontinuation of their administration are shown in Table 1.

Table 1. Body weight change in rats during the course of intragastric administration of the studied gel with astaxanthin and polyprenol and placebo, g

	Background	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	Hungry mass
Antioxidant gel with astaxanthin and polyprenols								
N	6	6	6	6	6	3	3	6
M±m	183±80,02	197±63,79	205±75,09	217±69,41	236±65,39	250±54,01	260±37,42	252±80,02
t	-1,07	-1,24	-1,39	-1,77	-1,13	-3,76	-1,13	-1,65
p	0,31	0,24	0,20	0,11	0,31	0,01	0,31	0,13
Placebo								
N	6	6	6	6	6	3	3	6
M±m	186±62,04	195±62,06	2055±63,78	216±20,54	225,6±59,84	245±68,19	255±50,99	240±62,04
t	0,10	-0,08	0,08	0,08	-0,03	1,80	1,74	-0,19
p	0,92	0,94	0,94	0,94	0,98	0,13	0,14	0,86
Control								
N	3	3	3	3	3	1	1	3
M±m	187±93,57	200±88,06	218±67,99	239±43,33	255±49,05	260±18,09	256±12,11	243±93,57
W	0,95	0,95	0,97	0,98	0,97	0,98	0,94	0,89
p	0,41	0,31	0,84	0,94	84,96	0,95	0,55	92,56

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat body mass parameter exceed the tabular value. Thus, when W = > Table. The distribution is normal, the hypothesis H_0 is accepted.

The body weight gain at 5 weeks in experimental animals treated with asntioxidant gel with astaxanthin and polyprenol and placebo differed slightly from the body weight gain of control animals - body weight significantly increased by 4% and 6%, respectively, due to a decrease in feed intake, but, in the recovery period, the growth rates in the study groups leveled off and they did not significantly differ from the mass of control animals, which allows us to conclude about the equitoxicity of the studied drugs.

The daily intake of feed and water was calculated weekly. The amount of food and water consumed by rats receiving the above preparations did not statistically differ from the indicators of animals in the control groups (Table 2.3).

Table 2. Daily feed intake in rats when using antioxidant gel with astaxanthin and polyprenol and placebo, g

	Background	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks
Antioxidant gel with astaxanthin and polyprenols							
N	6	6	6	6	6	3	3
M±m	22,5±4,52	19,37±3,75	26,5±1,67	29±2,41	21,75±2,69	18,67±6,41	23,33±4,08
t	0,00	-0,99	1,18	1,06	1,13	-1,17	-0,04
p	1,00	0,34	0,27	0,31	0,29	0,30	0,97
Placebo							
N	6	6	6	6	6	3	3
M±m	21,5±2,54	27,5±4,74	19,5±2,66	25,5±1,77	22,6±3,41	17,0±3,54	22,3±4,81
t	-0,22	0,32	-0,66	0,15	0,57	-2,31	-0,15
p	0,83	0,75	0,52	0,88	0,58	0,07	0,89
Control							
N	3	3	3	3	3	1	1
M±m	25,5±5,00	25,0±7,45	21,75±5,74	23,75±6,40	23,75±8,62	20±6,32	20±6,25
W	0,94	0,92	0,88	0,90	0,91	0,88	0,92
p	0,26	0,10	0,01	0,03	0,07	0,14	0,40

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H_0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

Table 3. Daily water intake in rats when using the studied drug and placebo, ml

	Background	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks
Антиоксидантный гель с астаксантином и полипренолом							
N	6	6	6	6	6	3	3
M±m	34,0±4,05	32,5±4,29	35,0±5,25	25,0±2,86	32,8±4,46	31,7±5,40	31,7±8,90
t	-0,35	-2,04	-1,03	-0,52	-0,21	4,08	1,72
p	0,73	0,07	0,33	0,62	0,84	0,01	0,15
Placebo							
N	6	6	6	6	6	3	3
M±m	31,5±2,67	32,1±2,46	30,6±2,93	31,2±1,86	32,9±3,97	31,3±11,37	32,3±4,81
t	0,39	-1,78	-0,43	-0,20	-0,52	1,34	1,88
p	0,71	0,11	0,67	0,85	0,61	0,24	0,12
Control							
N	3	3	3	3	3	1	1
M±m	30,0±2,44	32,0±3,33	32,5±2,87	31,5±5,0	31,2±6,21	30±10,12	31±11,31
W	0,91	0,88	0,94	0,90	0,92	0,95	0,89
p	0,06	0,02	0,29	0,05	0,11	0,61	0,16

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H_0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

The data of daily water consumption differed slightly at the period of 5 weeks - significantly increased by 6% in experimental animals treated with antioxidant gel with astaxanthin and polyprenol, due to the effect of the drug on the physiological functions of the body, namely, increased diuresis, which is consistent with stress effects, but, in the recovery period, daily water consumption in experimental animals animals receiving the drug and experimental animals

receiving placebo differed slightly from the consumption rate in control animals- significantly decreased by 4% and 3%, respectively, due to the stabilization of physiological functions of the body after discontinuation of the drug, which allows us to conclude about the equitoxicity of the studied drugs.

Effect on peripheral blood parameters

Peripheral blood parameters in animals treated with astaxanthin gel and polyprenols and placebo are presented in Table 4,5,6.

Table 4. The effect of the studied gel with astaxanthin and polyprenols and placebo on the composition of peripheral blood in rats, (M±m) (background)

	RBC, *10^{12}//l (number of red blood cells)	HGB, g/l (hemoglobin)	HCT, % (hematocrit)	MCV, fl (average red blood cell volume)	MCH, pg (average hemoglobin content in erythrocyte)	MCHC, g/l (cf. end of hemoglobin in the erythrocyte)	RDW, mmol/l (width of red blood cell distribution)	WBC, % (number of white blood cells)	Sticks, %	Segments, %	Eosinophils, %	Basophils, %	Monocytes, %	Lymphocytes, %	PLT, % (platelet count)	MPV, % (cf. platelet count indicator)
Antioxidant gel with astaxanthin and polyprenols																
N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
M ± m	4,8 ±0,3	85,7±7,2	24,2±3,9	50,9±1,2	20,2 ±0,9	346,9±18,8	35,6±1,4	17,3±3,9	1±0,2	51,9±4,7	1,6±0,3	3,0±0,3	42,6±4,7	433,1±691	6,4 ±0,4	4,8±0,3
t	-2,72	-0,96	-0,97	-0,30	2,13	0,72	-0,92	1,61	0,78	0,64	0,29	-1,49	0,86	-0,71	-1,89	-0,09
p	0,02	0,36	0,35	0,77	0,06	0,49	0,38	0,14	0,45	0,54	0,78	0,17	0,41	0,50	0,09	0,93
Placebo																
N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
M ± m	6,2 ±0,5	130,6±1(,6	27,6±2,8	52,9±0,6	31,2± 4,3	358,5± 7,9	38,3± 1,4	8,9 ±0,9	1±0,3	46,6±2,9	1,6±0,3	1,6±0,3	49,1± 3,3	346,1±40 6	6,97±0,1	6,2± 0,5
t	0,13	2,27	-0,47	0,36	2,41	1,91	-0,06	0,06	0,59	-0,19	0,25	-1,49	-1,52	0,32	-3,76	1,14
p	0,90	0,05	0,65	0,73	0,04	0,09	0,96	0,95	0,57	0,86	0,81	0,17	0,16	0,76	0,00	0,28
Control																
N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
M ± m	6,1± 0,4	96,2±8,3	29,7±3,8	51,8± 4,9	17±1,3	326,3± 22,5	38,5± 4,2	8,8 ±1,7	0,7±0 3	47,5±4,3	1,5±0,3	2,5±0,7	47,5± 4,5	638,0±94,0	6,45±0,7	6,1± 0,4
W	0,97	0,96	0,98	0,91	0,76	0,97	0,95	0,77	0,77	0,96	0,74	0,24	0,88	0,96	0,98	0,93
p	0,82	0,51	0,93	0,06	0,00	0,83	0,40	0,00	0,00	0,61	0,00	0,00	0,02	0,59	0,93	0,18

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = > Table. The distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

Table 5. The effect of the studied antioxidant gel with astaxanthin and polyprenols and placebo on the composition of peripheral blood in rats, (M=m) (after 14 days)

	RBC, *10^{12}//l (number of red blood cells)	HGB, g/l (hemoglobin)	HCT, % (hematocrit)	MCV, fl (average red blood cell volume)	MCH, pg (average hemoglobin content in erythrocyte)	MCHC, g/l (cf. end of hemoglobin in the erythrocyte)	RDW, mmol/l (width of red blood cell distribution)	WBC, % (number of white blood cells)	Sticks, %	Segments, %	Eosinophils, %	Basophils, %	Monocytes, %	Lymphocytes, %	PLT, % (platelet count)	MPV, % (cf. platelet count indicator)
Antioxidant gel with astaxanthin and polyprenols																
N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
M ± m	4,1 ±0,6	77,1±12,8	22,2±3,1	54,3±1,6	18,3±1,4	337,6±3,5	38,4±1,4	2,8±4,4	0,9 ±0,2	57,9±4,9	1,6±0,3	2,3±0,3	37,3±4,9	331,4±85,9	6,9 ±0,2	4,1±0,6
t	-2,08	0,15	-1,41	1,01	0,94	0,00	-0,34	0,46	-0,29	0,48	0,90	-0,51	0,38	-0,52	-0,67	0,85
p	0,06	0,89	0,19	0,34	0,37	1,00	0,74	0,66	0,78	0,64	0,39	0,62	0,71	0,62	0,52	0,42
Placebo																
N	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
M ± m	5,5 ±0,6	126,6±13,9	30,1±3,3	54,9 ±0,5	24,9 ±4,9	455,3 ±91,8	40,4±1,4	8,6 ±1,4	0,8 ±0,3	59,5±4,4	1,4±0,3	1,8±0,4	36,5±4,3	346,1±40,6	6,98±0,1	5,5±0,6
t	-0,45	2,52	0,26	1,88	1,30	0,92	0,71	-0,56	-0,55	0,77	0,30	-0,51	-0,33	-0,70	-0,86	1,15
p	0,67	0,03	0,80	0,09	0,22	0,38	0,49	0,59	0,59	0,46	0,77	0,62	0,75	0,50	0,41	0,28
Control																
N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
M ± m	5,8 ±0,3	74,3±14,7	28,9±3,6	51,5±,9	16,1±2,3	337,8±10,9	39,1±0,95	9,95 ±2,5	1,0±0,5	54,5±4,4	1,3±0,3	2,0±0,8	41,0±4,9	872,0±459,8	6,7 ±0,4	5,8±0,3
W	0,92	0,97	0,95	0,84	0,56	0,50	0,84	0,87	0,80	0,95	0,67	0,43	0,81	0,97	0,96	0,98
p	0,11	0,78	0,36	0,00	0,00	0,00	0,00	0,01	0,00	0,34	0,00	0,00	0,00	0,72	0,46	0,86

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

Table 6. The effect of the studied antioxidant gel with astaxanthin and polyprenols and placebo on the composition of peripheral blood in rats, (M=m) (after 14d+2 weeks)

	RBC, *10^{12}//l (number of red blood cells)	HGB, g/l (hemoglobin)	HCT, % (hematocrit)	MCV, fl (average red blood cell volume)	MCH, pg (average hemoglobin content in erythrocyte)	MCHC, g/l (cf. end of hemoglobin in the erythrocyte)	RDW, mmol/l (width of red blood cell distribution)	WBC, % (number of white blood cells)	Sticks, %	Segments, %	Eosinophils, %	Basophils, %	Monocytes, %	Lymphocytes, %	PLT, % (platelet count)	MPV, % (cf. platelet count indicator)
Antioxidant gel with astaxanthin and polyprenols																
N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
M ± m	6,9 ±0,7	129,6±14,6	37,8±3,8	54,4±2,2	18,3±1,1	333,2±15,9	41,1±0,6	20,8±5,4	0,6±0,3	48,1±5,9	1,9±0,4	0,93±0,2	48,5±5,7	579,4±946	6,9 ±0,2	6,9±0,7
t	1,44	1,06	1,53	-0,06	-1,04	-1,45	0,61	0,84	-2,05	-1,07	-0,62		-0,29	1,26	-0,32	1,10
p	0,18	0,31	0,16	0,95	0,32	0,18	0,55	0,42	0,07	0,31	0,55		0,78	0,24	0,76	0,30
Placebo																
N	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
M ± m	4,8 ±0,5	97,0±13,0	27,7±3,3	53,0±2,0	18,96±0,9	351,6±14,4	40,4±0,97	7,12±1,4	1,0±0,3	65,6±5,4	1,9±0,4	1,0±0,3	30,5±5,3	339,5±46,2	6,9 ±0,2	4,8±0,5
t	-0,84	-0,63	-0,43	-0,48	-0,71	-0,65	0,03	-2,28	-0,98	1,15	-0,57		0,00	-1,01	-2,42	1,25
p	0,42	0,55	0,67	0,64	0,49	0,53	0,97	0,05	0,35	0,28	0,58		1,00	0,34	0,04	0,24
Control																
N	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
M ± m	5,4 ±0,3	108,3 ±6,3	29,7±1,6	54,6±3,2	19,95±1,1	364,52±3,5	40,4±1,4	14,3 ±4,3	1,5±0.	57,0±3,4	2,3±0,6	1,0±0,5	38,3±4,5	631,3±17,0	6,6 ±0,2	5,4±0,3
W	0,92	0,94	0,94	0,80	0,96	0,80	0,99	0,84	0,84	0,95	0,81		0,80	0,98	0,92	0,95
p	0,10	0,22	0,24	0,00	0,64	0,00	1,00	0,00	0,00	0,42	0,00		0,00	0,90	0,12	0,42

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (W calculation) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W is calculated › W is Table. The

distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

A significant increase in leukocytes by 15% in experimental animals treated with antioxidant gel with astaxanthin and polyprenol and a decrease by 9% in experimental animals treated with placebo in blood plasma compared with control animals indicates the manifestation of effects as a result of 14-day use of the studied drugs. In animals of all experimental groups, after a 14-day course of taking the studied drugs, there are no pathological shifts in the leukocyte nucleus and a significant change in the hematological profile, which allows us to conclude about the equitoxicity of the studied antioxidant gel with astaxanthin and polyprenol and placebo.

After discontinuation of the administration of drugs (recovery period - 2 weeks) and hematological examination, no significant differences were found between the studied gel and placebo. There was a slight significant increase in segmented neutrophils (by 11.3% in the group of experimental animals receiving placebo and by 6% in the group of experimental animals receiving antioxidant gel with astaxanthin and polyprenol compared with the indicators of control animals), which is not associated with a reaction to drugs and indicates the absence of delayed toxic effects. The decrease in hemoglobin content in erythrocytes by 4.7% in the group of experimental animals receiving placebo and by 5% in the group of experimental animals receiving gel with astaxanthin and polyprenol was caused by the stabilization of previously altered hemodynamic parameters when using the studied drug.

Thus, the peripheral blood of rats of all experimental groups after 30 days of administration of the tested antioxidant gel with astaxanthin and polyprenol corresponded to the specific physiological norm in its quantitative and qualitative composition and no significant differences between the studied drug 1 and the placebo drug were revealed.

Influence on blood biochemical parameters

Table 7, 8, 9 presents data on the effect of the studied preparation of an antioxidant gel with astaxanthin and polyprenol and placebo on the main biochemical parameters and on the activity of rat blood enzymes. The study was carried out on a biochemical automatic analyzer ILAB 650 (USA).

Table 7. The effect of the studied preparation Antioxidant gel with astaxanthin and polyprenols and placebo on the main biochemical parameters of the peripheral blood of rats, (background) (M±m)

	Urea, mmol/l	Creatinine, mmol/l	Total bilirubin, mmol/l	AST, units/l	ALT, units/l	SCHF, units/l	Glucose, mmol/l	Total protein, g/l	Direct bilirubin, units/l	LDG, units/l	Amylase, units/l
Antioxidant gel with astaxanthin and polyprenols											
N	6	6	6	6	6	6	6	6	6	6	6
M±m	9,9±0,5	140,6±6,1	5,4±0,6	58,3±3,1	85,1±5,8	65,4±5,0	5,7±0,4	68,3±2,8	1,1±0,1	202,6±13,5	150,4±10,7
t	0,63	4,31	-0,67	-2,10	2,23	-2,78	0,27	1,43	1,51	-0,06	0,69
p	0,54	0,00	0,52	0,06	0,05	0,02	0,79	0,18	0,16	0,95	0,51
Placebo											
N	6	6	6	6	6	6	6	6	6	6	6
M±m	9,6±0,6	126,3±6,4	6,3±0,4	63,6±5,9	71,9±4,6	105,8±10,1	5,97±0,2	68,4±4,2	0,9±0,05	210,9±15,2	145,3±3,4

t	0,19	2,83	0,46	-0,66	1,20	1,25	0,95	1,12	0,46	0,34	0,72
p	0,85	0,02	0,66	0,53	0,26	0,24	0,36	0,29	0,66	0,74	0,49
Control											
N	3	3	3	3	3	3	3	3	3	3	3
M±m	9,4±0,6	96,0±10,89	6,1±0,6	69,3±5,4	59,3±14,7	87,8±7,4	5,6±0,5	61,0±5,8	0,9±0,1	203,8±7,3	139,3±11,8
W	0,95	0,97	0,96	0,98	0,96	0,93	0,89	0,95	0,78	0,96	0,97
p	0,39	0,66	0,63	0,96	0,63	0,12	0,02	0,33	0,00	0,52	0,82

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

Table 8. The effect of the studied antioxidant gel with astaxanthin and polyprenols and placebo on the main biochemical parameters of the peripheral blood of rats, (after 14 days) (M=m)

	Urea, mmol/l	Creatinine, mmol/l	Total bilirubin, mmol/l	AST, units/l	ALT, units/l	SCHF, units/l	Glucose, mmol/l	Total protein, g/l	Direct bilirubin, units/l	LDG, units/l	Amylase, units/l
Antioxidant gel with astaxanthin and polyprenols											
N	6	6	6	6	6	6	6	6	6	6	6
M±m	8,7±0,7	165,8±7,9	6,1±0,3	92,4±16,1	59,4±6,2	54,3±4,8	3,7±0,6	74,4±2,2	1,3±0,1	289,9±29,1	113,4±10,1
t	1,37	0,89	1,79	-0,19	-0,52	-2,15	-2,41	1,54	0,36	0,95	-2,66
p	0,20	0,40	0,11	0,85	0,61	0,06	0,04	0,16	0,73	0,36	0,02
Placebo											
N	6	6	6	6	6	6	6	6	6	6	6
M±m	9,3±0,8	174,4±4,5	5,7±0,4	72,5±10,0	72,5±11,0	69,0±10,3	4,9±0,4	83,3±2,8	1,1±0,1	231,1±20,7	168,6±24,6
t	1,71	1,66	0,58	-1,63	0,14	-0,07	-1,60	2,60	-0,83	-0,63	-0,49
p	0,12	0,13	0,57	0,14	0,88	0,95	0,14	0,03	0,43	0,54	0,64
Control											
N	3	3	3	3	3	3	3	3	3	3	3
M±m	6,9±1,4	151,5±17,9	5,4±0,3	96,8±9,3	69,3±25,2	70,0±4,9	5,9±0,4	63,0±10,1	1,23±0,09	250,5±18,2	189,0±37,1
W	0,92	0,93	0,97	0,96	0,83	0,88	0,94	0,91	0,97	0,98	0,82
p	0,11	0,16	0,74	0,49	0,002	0,015	0,24	0,06	0,78	0,94	0,002

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905.

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

There was a significant decrease in glucose and amylase levels in animals treated with the studied drug - antioxidant gel with astaxanthin and polyprenol and placebo (glucose -17%, amylase -32%), as well as a significant increase in protein content in animals treated with placebo by 32% relative to control, indicating a pancreatic reaction, circulatory and hemodynamic changes due to prolonged use (1 month).

Table 9. The effect of the studied antioxidant gel with astaxanthin and polyprenols and placebo on the main biochemical parameters of the peripheral blood of rats, (after 14 days +2 weeks) (M=m)

	Urea, mmol/l	Creatinine, mmol/l	Total bilirubin, mmol/l	AST, units/l	ALT, units/l	SCHF, units/l	Glucose, mmol/l	Total protein, g/l	Direct bilirubin, units/l	LDG, units/l	Amylase, units/l
Antioxidant gel with astaxanthin and polyprenols											
N	3	3	3	3	3	3	3	3	3	3	3
M±m	8,6±1,2	131,3±14,2	5,6±0,3	103,3±33,3	60,0±27,0	48,7±24,1	5,9±0,8	72,0±5,3	1,2±0,1	276,0±34,8	116,0±10,4
t	1,05	-0,47	1,02	0,30	-0,26	-1,54	0,10	0,12	-0,41	0,04	-1,39
p	0,34	0,66	0,35	0,77	0,80	0,18	0,92	0,91	0,70	0,97	0,22
Placebo											
N	3	3	3	3	3	3	3	3	3	3	3
M±m	7,4±0,8	127,7±10,1	5,8±0,4	69,3±26,60	50,7±4,3	43,3±17,0	6,6±0,4	78,0±12,3	1,2±0,3	294,3±15,1	123,0±17,3
t	0,37	-0,65	1,32	-1,20	-0,62	-2,63	1,42	0,61	-0,33	0,89	-1,04
p	0,73	0,55	0,24	0,28	0,56	0,05	0,21	0,57	0,76	0,41	0,34
Control											
N	1	1	1	1	1	1	1	1	1	1	1
M±m	6,95	125	4,7	70	54	73	5,8	72	1,4	307	132
W	0,94	0,85	0,96	0,97	0,72	0,90	0,91	0,94	0,98	0,97	0,84
p	0,55	0,06	0,76	0,93	0,00	0,24	0,29	0,58	0,94	0,89	0,04

*At the significance level α=5% and n=15, the tabular value of the Shapiro-Wilk criterion (W Table)=0,905/

The calculated values of the criterion (Rr.) for the parameters of the rat feed consumption parameter exceed the tabular value. Thus, when W = › Table. The distribution is normal, the hypothesis H0 is accepted (see Appendix). The obtained empirical values of the Student's T-test are in the zone of insignificance.

There was a significant decrease in glucose and amylase levels in animals treated with the studied drug - antioxidant gel with astaxanthin and polyprenol and placebo (glucose -17%, amylase -32%), as well as a significant increase in protein content in animals treated with placebo by 32% relative to control, indicating a pancreatic reaction, circulatory and hemodynamic changes due to prolonged use (14 days).

During the recovery period (14 days after the end of the drug administration), a decrease in the alkaline phosphatase index (by 41%) was observed in animals receiving placebo, in animals receiving the studied drug - an antioxidant gel with astaxanthin and polyprenol, the previously changed indicators (glucose, amylase) did not significantly differ from those in the control animal group, all the indicators have stabilized.

As can be seen from the data presented above, both the studied and placebo drugs in the tested dose do not have a sharply negative effect on the basic biochemical parameters of blood and the activity of plasma enzymes.

Study of possible local irritant action

With intragastric administration of the studied drugs, there were no signs of a local inflammatory reaction of the mucous membrane of the gastrointestinal tract (infiltration, redness), which was confirmed by visual and histological examination.

Examination of the gastric mucosa – the stomach wall is represented by mucous, muscular and serous membranes, the villi of the mucosa are high, the pituitary-cervical sections are not

deepened, uniform distribution of glands, pathological changes of the mucous membrane (hyperemia, edema, erosion) are not revealed. *Examination of the intestinal mucosa (12-digit, thin and thick intestine)* – the muscular membrane is represented by bundles of smooth muscle fibers, the serous membrane is formed by connective tissue and covered with mesothelium, without defects, folding is preserved, the mucous membrane of the small intestine is represented by a single-layer cylindrical epithelium, a wide brush border and multiple goblet cells, crypts are preserved. Intestinal villi without atrophy, all layers of the intestine (own mucosal plate, muscle membrane, serous membrane) without pathological changes (hyperemia, edema, erosion). The serous membrane is formed by a thin connective tissue and is covered with mesothelium. The mucous membrane of the large intestine is without defects, formed by a single-layer cylindrical epithelium, lined with goblet-shaped cells, has parallel crypts. The muscle membrane is formed by the inner circular and outer longitudinal layers of myocytes. The serous membrane is formed by a thin connective tissue and is covered with mesothelium.

No local inflammatory reaction was detected after intragastric administration of drugs (Table 10).

Table 10. Registration of local inflammatory reaction in rats after administration of antioxidant gel with astaxanthin and polyprenol and placebo

Medication	Reaction on time	
	14 days, points (n=3)	14 days+2 weeks, points (n=3)
Antioxidant gel with astaxanthin and polyprenols (n=6)	0	0
Placebo (n=6)	0	0

The histological picture obtained during this study allows us to judge the absence of a local irritant effect in the studied gel with astaxanthin and polyprenol and placebo, which does not exclude the possibility of developing a reaction with individual sensitivity of the body in humans.

4. Conclusion.

In an experimental study on laboratory animals, no local inflammatory reaction was recorded, as well as pathological changes in hematological and biochemical parameters of blood, which indicates the absence of toxicity and local irritating effect of the antioxidant gel with astaxanthin

Application of artificial intelligence: The article is written without the use of artificial intelligence technologies.

Conflicts of Interest: The authors declare no conflict of interest

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Article

Cephalometric Analysis in Studying the Position of the Hyoid Bone and the Upper Respiratory Tract Status in Patients with Occlusion Issues.

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Abstract:

Rationale. Occlusion sagittal issues come accompanied with morphological disorders affecting the facial skeleton, the shape and size of dental arches, the temporomandibular joint elements, disturbed chewing function, swallowing, breathing, speech production, as well as change involving the posture balance. Cephalometric analysis offers the most reliable and promising option in studying the hyoid bone position and the upper respiratory tract (URT) status.

Aim of study. This study was carried out aiming at improving the diagnostics reliability, when dealing with patients featuring occlusion pathology, through studying the hyoid bone position and the upper respiratory tract status relying on the cephalometric analysis of the head lateral telerentgenograms (TRG).

Materials and methods. The study involved 76 children aged 15-17 bearing the diagnosis of *Distal occlusion* (DO); the patients were divided into 2 subgroups – Subgroup 1 (n=41) where the patients had DO combined with sagittal incisive disocclusion and Subgroup 2 (n=35) who featured DO along with deep incisive disocclusion. Adolescents (n=34) revealing physiological occlusion were the comparison group. The cephalometric analysis of the head profile TRGs (OnDemand3D™ Dental software; CEPH module) employed linear, angular and index parameters in order to identify individual features of the craniofacial structure as well as the os hyoideum position. The degree of the URT narrowing at the nose and oropharynx level was determined via 3D reconstruction of cone beam computed tomograms (CBCT) based on a visual colorimetric scale.

Results and discussion. The cephalometric analysis of the linear, angular and index indices of the head lateral TRGs obtained through examining adolescents with distal occlusion revealed mutual effects of gnathic, cranial and dental alveolar factors. The hyoid bone upward displacement in adolescents with DO, if compared to children with physiological occlusion, was obvious through a statistically significant ($p \leq 0.05$) decrease in the Me values of H-S (by 13.69%-14.55%); H-RGn (by 21.91%-22.57%); H-MR (by 47.57% and 54.76%); ‹H-Me-MP (by 32.38%-34.98%). As far as the os hyoideum backward shift is concerned, it was to be seen from a significant ($p \leq 0.05$) decrease in the Me values of H-C_{III} (by 25.42%-26.05%) with an increase in ‹HGo-NM (by 9.94%-10.34%). The changes identified in the hyoid bone topography in children with DO came combined with a dynamic narrowing of the URT, that manifesting itself through a significant ($p \leq 0.05$) reduction in the total volume of the respiratory tract and the cross-sectional area.

Conclusion.The URT volume measurement carried out with CBCT, the hyoid bone topography evaluation, identifying the tongue position and size along with doing the same for the cervical vertebrae and for the posture compensation degree, allow the dentist to take an objectively reliable approach to diagnosing and treating dental pathologies, which, in turn, will improve the overall quality of dental treatment. The retroposition of the lower jaw results in a compressed upper respiratory tract, which will facilitate the development of compensatory changes in the cranio-vertebral joint, that expressing in the anterior position of the head. Identifying due normative parameters and the status of the URT, as well as the connection with the dental structure status, for cases falling within norm or disturbed occlusion range, will require further research.

Keywords: cone beam computed tomography, upper respiratory tract, cephalometric analysis, hyoid bone position, distal occlusion, lateral telerentgenogram, craniofacial area.

1. Introduction

The current progress in fundamental science and the widespread introduction of innovation-based technologies into Medicine nowadays offer many more options for employing in vivo imaging methods, both in anatomical and topographic & anatomic studies [1-5].

Advanced study of morphological and topographic features, dimensional values, individual anatomic variability of the hyoid bone structure, as well as links with the craniofacial region structures and ENT organs is of great research and applied importance for otorhinolaryngology, maxillofacial surgery, surgical dentistry, orthognathic surgery, orthodontics, and forensic medicine [5-8].

The hyoid bone, as an element connecting the neck deep muscles and the oral cavity bottom, plays an important role in swallowing, speech production, complex head turns, whereas clinicians' lacking knowledge of the hyoid bone typical anatomy and topography, in view of the constitution type, may serve a serious obstacle when diagnosing closed neck injuries, increase the risk of damage to vital organs, as well as make it difficult to perform successful intubation, as well as lead to internal injuries of the larynx and trachea during medical procedures and manipulations [9,10].

The focus of otorhinolaryngologists' and dentists' attention is the respiratory tract status, viewed as one of the key factors behind the growth and development of maxillofacial structures [11].

Given the functional integrity of the craniofacial area anatomical structures, experts do not identify the primary etiopathogenetic mechanism, which results in obstructed upper respiratory tract or dental anomalies. On the one hand, the functional imbalance arising from the nasopharyngeal tonsils hypertrophy, curved nasal septum, foci of chronic infection affecting the ENT organs, allergic rhinitis, nasal polyps, and congenital abnormalities involving internal organs contribute to the development of oral breathing, disturbed tightness of the oral cavity with lacking negative pressure in it; non-physiological (lower) position of the tongue; muscle discoordination resulting in the posterior position of the lower jaw; the vertical type of the facial skeleton growth; narrowing upper dental arch in the distal – and elongated in the frontal – sections. On the other hand, dental anomalies caused by maxillofacial malformations due to growth issues in the embryonic period, functional disorders of chewing and facial muscles, adverse external factors and poor habits through the period of developing the temporary and permanent bite, change the

physiological ratio of the head, jaw bones and tongue, initiating narrowing (stenosis) of the airways [12-20].

Identifying the upper respiratory tract (URT) status employing the skull TRG in the lateral projection allows obtaining details regarding the width of the lumen along the sagittal. The authors of the study have proposed various methods for assessing the URT patency, which differ in the number (topography) of the reference points (lines) and the measurement levels of cross-sections [21,22]. Despite the controversial issues in detecting the URT boundaries due to the variability and mobility of soft tissues and bone structures around the respiratory tract, as well as to the normative values of the URT lumen in various areas, respiratory failures can be diagnosed in case of a 40+% reduction in the URT cross-sectional area [23].

High-tech radiation methods, such as computed tomography (CT) and magnetic resonance imaging (MRI) allows performing 3D diagnostics of URT while maintaining the volume of the object and the possibility of post-contrast thin-slice imaging in any of the planes at high resolution, taking into account contour irregularities [24-27]. 3D reconstruction with cone beam computed tomography (CBCT), which features a lower radiation load, is the most reliable and diagnostically valuable method of measuring URT; besides, unlike MRI, CBCT offers an advantage in assessing the status of bone structures and foreign bodies [28-30]. The reference points that are described in the scientific literature, which allow identifying linear and angular parameters for assessing the hyoid bone topography in patients with dental anomalies, are not numerous and of a disparate nature, which was the reason explaining the rationale of this study.

Aim of study: to study the topography of the hyoid bone in adolescents with distal occlusion, while relying on cephalometric analysis of head telerentgenograms (TRG) in the lateral projection.

2. Patients and Methods

The premises of the Orthodontic Department (Pediatric Dental Polyclinic, Stavropol State Medical University / StSMU) and of the Department for General Practice Dentistry and Pediatric Dentistry of StSMU were used (2018-2023) to carry out a clinical X-ray examination and comprehensive treatment involving 76 patients (29 males, 47 females) with gnathic distal occlusion of the dentition caused by inferior micrognathia and posterior position of the lower jaw (main group). The inclusion criteria for the main group were: age – 15-17; distal occlusion (K07.20 by ICD-10); mandible micrognathia (K07.04 by ICD-10); mandible retrognathia (K07.13 by ICD-10); skeletal II class by E. Angle (∠SNB value less than 78°, ∠ANB value more than 4°); ratios for the first molars - more than 1 mm; incisor retraction; incisor protrusion; informed voluntary consent obtained from the patients' parents (legal representatives) for orthodontic treatment; no congenital maxillofacial malformations; no bone diseases; no mental disorders.

The diagnosis was set relying on the outcomes of clinical and additional re-search methods. Based on the classification of abnormal dentition occlusion(by Prof. L.S. Persina, Member of the Russian Academy of Medical Sciences, 1989), subject to a recommendation by the resolution of the X Congress of the Russian Professional Society of Orthodontists (2006), the patients of the main

group were divided into two subgroups: Subgroup 1 – children with distal occlusion accompanied by sagittal incisive disocclusion (n=41; 13 - males, 28 – females); Subgroup 2 – children with distal occlusion accompanied by deep incisive disocclusion (n=35; 14 - males, 21 – females). The comparison group (n=34; 12 - males, 22 – females) included patients with

physiological types of occlusive relationships (of similar age) (Class I by E. Angle, ∠SNB – 80±2°, ∠ANB – 2±2°).

Since there was no statistically significant difference resulting from the gender, cephalometric studies data obtained in females and males were combined. X-Ray examinations (OPTG, TRG of the head in the lateral projection, CBCT) were performed employing a KaVo Orthopantomograph™ OP 3D digital X-ray diagnostic system with the 3D-tomography function with the conventional occlusion at standard head positioning in the cephalostat (radiation load – 1.8-3.1 microsievert). Further cephalometric analysis of the head TRG in the lateral projection (OnDemand3D Dental software, CEPH module) employed 39 values pertaining to the dental parameters, the skeletal status, as well as soft-tissue and skeletal profiles. Of the total number of parameters that serve to identify the individual dental morphological features, 11 linear, 10 angular and 2 index values were selected as the most significant in terms of diagnosing distal occlusion. To identify the alteration degree in the hyoid bone topography, 7 linear and 2 angular indicators describing the position of os hyoideum relative to the cervical spine and bones of the facial skull, were specifically identified (Table 1, Fig. 1-3).

Parameters	Title
Skeletal parameters	
Linear parameters (mm)	
N-Me	Anterior total morphological height of the face
N-ANS	Front upper face height
N-Se	Length of the anterior aspect of the skull base
N-Gn	Anterior height of the facial skull
A*-SnP	Upper jaw length
ANS-Me	Front lower face height
S-Go	Posterior face height
Pg-Go	Length of the base of the mandible
Co-Go	Length of the mandibular branch
H-S	Distance from the body of the hyoid bone to the equidistant point of the contour of the Turkish saddle
H-C_{III}	Distance from the body of the hyoid bone to the lowest point of the anterior edge of the body of the third cervical vertebrae
H-RGn	Distance from the body of the hyoid bone to the posterior point of the chin symphysis
H-MP	Length of the perpendicular from the body of the hyoid bone to the plane of the base of the mandibular body
H-N	Distance from the body of the hyoid bone to the anterior point of the nasolabial suture in the sagittal plane
H-A	Distance from the body of the hyoid bone to the distally located point on the anterior contour of the apical base of the maxilla
H-B	Distance from the body of the hyoid bone to the distally located point on the anterior contour of the apical base of the mandible
Index parameters (%)	
N-ANS/ANS-Me	Ratio of anterior upper to anterior lower face height
S-Go/N-Me	Ratio of posterior facial height to total anterior facial height
Angular parameters (°)	
‹SNB	Position of the apical base of the mandible relative to the anterior part of the skull base sagittally
‹SNA	Position of the apical base of the maxilla relative to the anterior part of the skull base sagittally
‹ANB	Ratio of the apical bases of the jaws relative to the skull base
‹Go	Angle of the mandible
‹SN-Pog	Anteroposterior position of the chin relative to the anterior skull base
‹Beta	Ratio of upper and lower jaws, skeletal class

‹NSe-MP	Position of the mandibular body base plane in relation to the length of the anterior skull base
‹NSe-SpP	Position of the plane of the base of the maxilla in relation to the length of the anterior skull base
Σ Bjork	Sum of angles by Bjork = ‹NSeAr + ‹SeArGo + ‹ArGoMe
‹H-Me-MP	Inclination of the body of the hyoid bone to the plane of the base of the mandibular body
‹HGo-HMe	Position of the body of the hyoid bone in relation to the plane of the base of the mandibular body
Dental parameters	
Linear parameters (mm)	
Overbite	Depth of cutter overlap
Overjet	Sagittal cleft size
Angular parameters (°)	
‹U1-L1	Interincisal Angle

Table 1. Linear, index and angular parameters studied at head TRG in lateral projection through cephalometric analysis

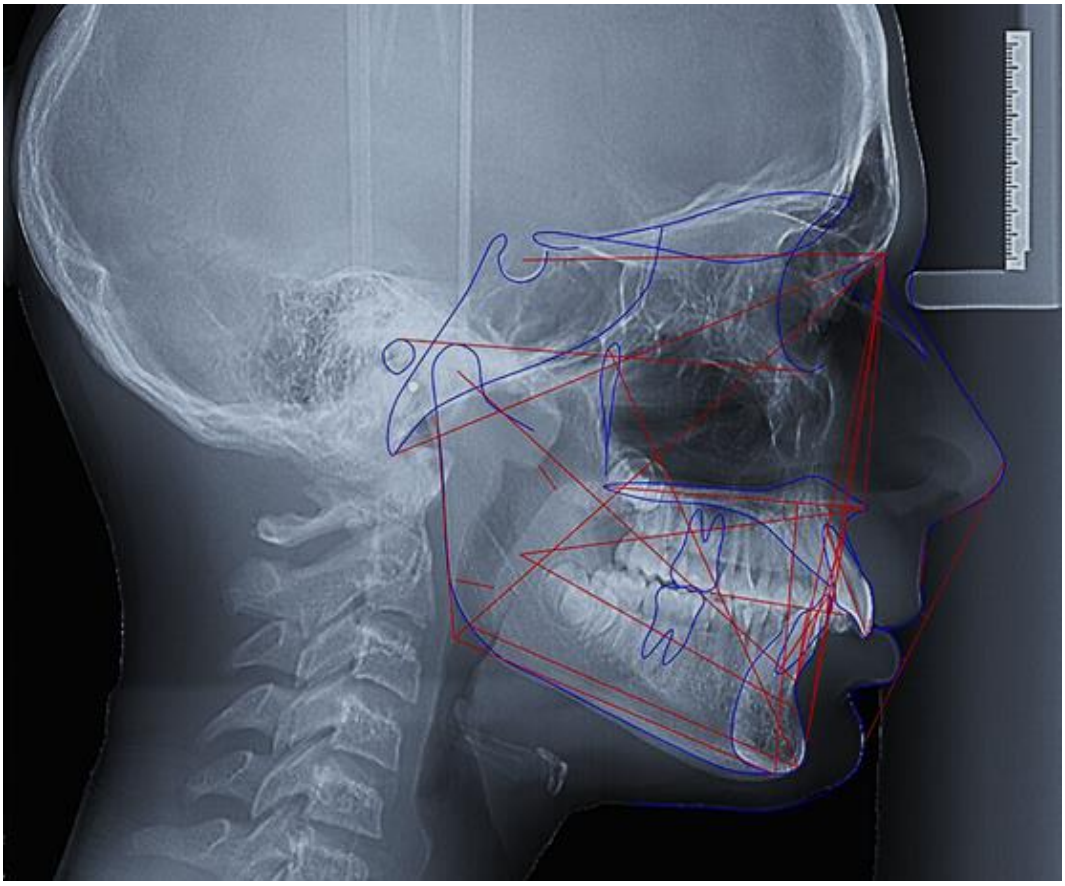

Fig. 1. Head TRG examination scheme; lateral projection; patient M., 16 y.o.; distal occlusion accompanied by deep incisive disocclusion.

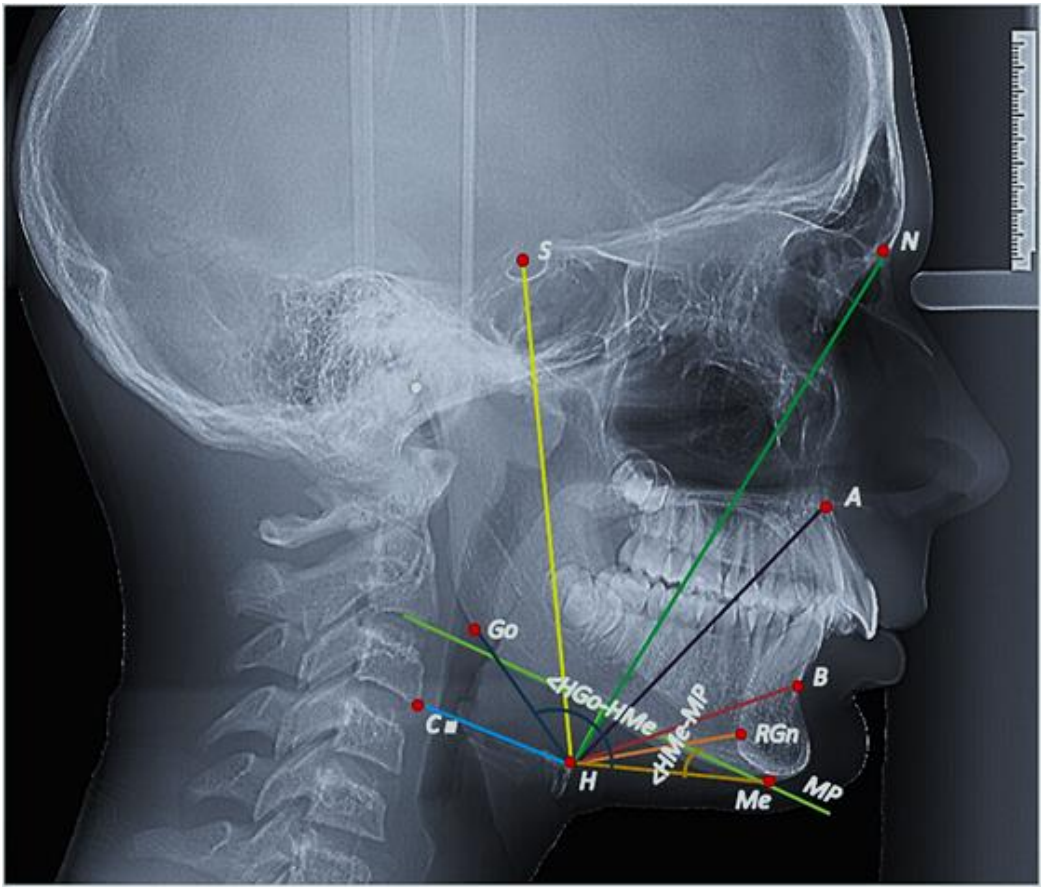

Fig. 2. Location of reference points, linear and angular parameters for determining the topography of the hyoid bone on a head TRG; lateral projection; patient M., 16 y.o.; distal occlusion accompanied by deep incisive disocclusion.

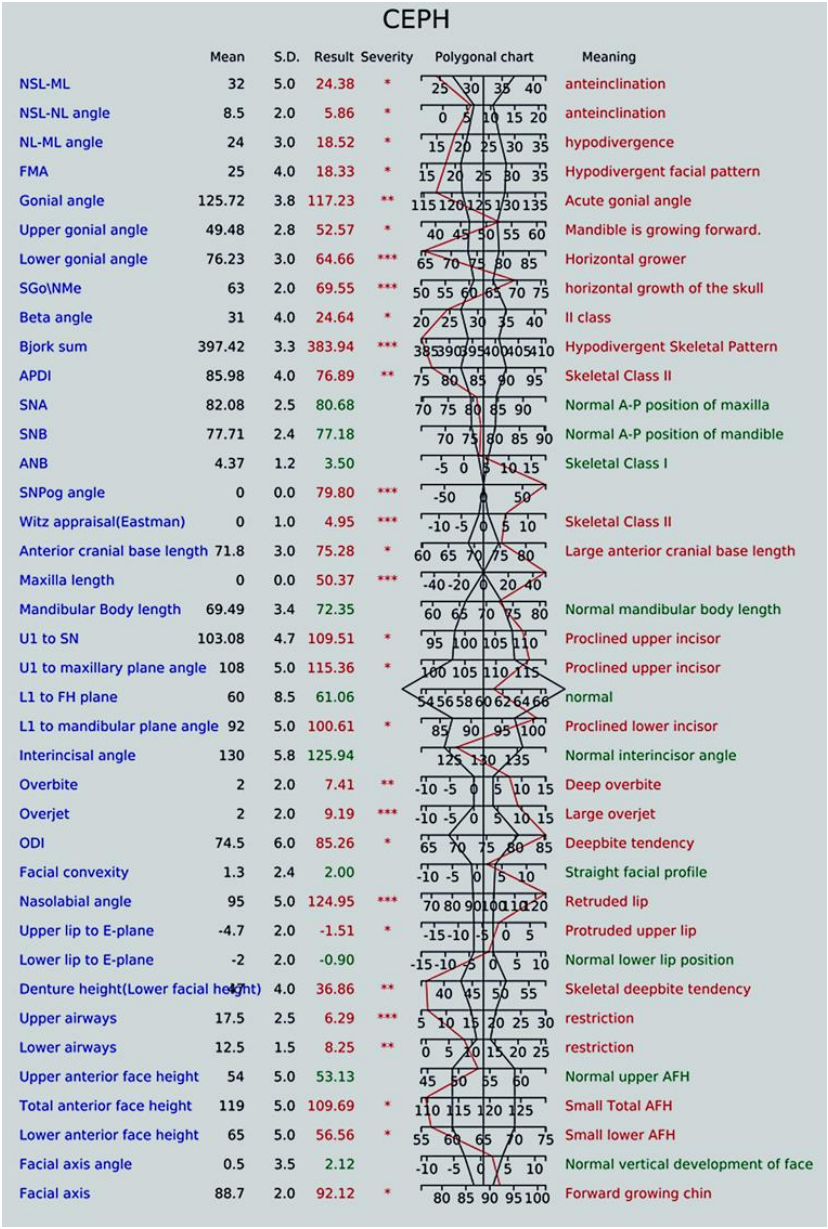

Fig. 3. Final computer analysis pattern of head TRG; lateral projection; patient M., 16 y.o.; with distal occlusion accompanied by deep incisive disocclusion (OnDemand3D™ Dental program, CEPH module).

The statistical analysis was performed using the Version 21.0 Microsoft Office Excel software package and Statistics 22.0 IBM ® SPSS ® (StatSoft Inc, USA). The hypothesis normality of the quantitative features distribution was checked through the Kolmogorov-Smirnov criterion employing the Lilliefors test as well as Shapiro-Wilk's test. The studied indicators predominantly had significant deviations from normality, so nonparametric criteria were used to identify the median (Me), minimum (Min) and maximum (Max) values, as well as the 10th, 25th (Q1), 75th (Q3), 90th percentiles. The comparisons of independent samples were set with the Mann–Whitney U test (the critical significance p level was taken as 0.05). Further pairwise comparison of the groups was performed using the Mann–Whitney U test with Bonferroni correction.

3. Results

Tables 2-4 contain the results of the head TRG cephalometric analysis in the lateral projection.

Table 2. Linear, index and angular parameters studied at head TRG in lateral projection; patients with physiological occlusion (comparison group)

Parameters	Me	Min	Max	Percentiles			
				Q-25	Q-75	Q-10	Q-90
Skeletal parameters							
Linear parameters (mm)							
N-Me	114,04	109,51	118,72	113,17	115,49	112,09	116,58
N-ANS	52,97	48,62	57,49	51,54	54,06	50,16	54,91
N-Se	69,75	64,43	75,22	68,03	71,64	66,71	73,83
N-Gn	124,52	116,77	130,04	122,09	126,14	118,82	127,95
A*-SnP	45,08	43,63	47,21	44,73	45,90	44,05	46,74
ANS-Me	64,82	60,19	69,13	63,18	65,91	61,56	66,84
S-Go	73,01	69,28	78,31	72,28	75,18	71,24	76,43
Pg-Go	72,46	67,93	79,07	71,84	74,65	69,04	76,99
Co-Go	53,18	49,27	57,01	51,77	54,43	50,36	56,14
Index parameters (%)							
N-ANS/ANS-Me	81,72	80,78	83,16	81,57	82,02	81,48	82,15
S-Go/N-Me	64,02	63,26	65,96	63,87	65,09	63,56	65,56
Angular parameters (°)							
‹SNB	79,67	75,94	84,13	78,52	81,05	77,26	82,81
‹SNA	82,14	78,06	89,19	80,89	84,02	79,93	85,44
‹ANB	2,26	-1,07	6,41	1,57	3,40	0,13	4,91
‹Go	129,58	122,94	137,65	126,83	132,16	125,02	134,59
‹SN-Pog	80,38	68,70	88,23	78,92	83,07	76,64	85,33
‹Beta	28,81	21,32	39,78	27,97	33,18	26,71	35,25
‹NSe-MP	31,07	27,15	38,36	29,94	33,53	28,89	35,70
‹NSe-SpP	8,28	4,63	12,06	7,06	10,15	5,94	10,82
Σ Bjork	393,41	379,54	401,12	390,73	395,24	383,76	399,62
Dental parameters							
Linear parameters (mm)							
Overbite	2,13	0,76	3,84	1,42	2,81	1,09	3,38
Overjet	2,46	0,54	5,12	1,56	3,31	1,23	4,04
Angular parameters (°)							
‹U1-L1	135,62	131,28	139,09	133,84	136,96	132,70	137,86

Table 3. Linear, index and angular parameters studied at head TRG in lateral projection; patients with distal occlusion accompanied by sagittal incisive disocclusion (Sub-group 1, main group)

Parameters	Me	Min	Max	Percentiles			
				Q-25	Q-75	Q-10	Q-90
Skeletal parameters							
Linear parameters (mm)							
N-Me	111,42	107,03	115,12	110,13	112,51	108,94	113,37
N-ANS	48,19**	43,97**	54,31**	47,34**	49,26**	46,01**	51,41**
N-Se	70,88	63,26	76,19	68,71	73,03	65,83	74,52
N-Gn	112,45	100,91	123,58	109,63	116,90	107,16	120,72

A*-SnP	50,37*	44,19*	57,04*	48,84*	52,05*	47,13*	54,28*
ANS-Me	65,38	60,76	71,12	64,48	66,61	63,24	68,74
S-Go	69,17	64,91	76,05	67,89	70,73	66,29	72,69
Pg-Go	73,76	65,52	80,93	72,01	75,92	68,39	78,24
Co-Go	57,24	49,83	64,65	55,69	59,19	53,18	62,07
Index parameters (%)							
N-ANS/ANS-Me	73,71	72,47	76,36	73,42	73,95	72,75	74,79
S-Go/N-Me	62,08	60,65	66,06	61,64	62,86	60,85	64,12
Angular parameters (°)							
‹SNB	73,05**	69,59**	77,18**	72,14**	74,49**	71,08**	75,91**
‹SNA	82,39	77,81	90,58	81,07	84,51	79,14	87,08
‹ANB	5,95	4,17	8,22	5,16	6,54	4,42	7,13
‹Go	120,27	113,96	126,42	118,89	121,93	117,16	124,51
‹SN-Pog	76,57	67,11	84,83	74,20	79,05	72,39	82,44
‹Beta	19,86*	16,32*	23,07*	18,73*	20,77*	17,64*	21,49*
‹NSe-MP	28,38	25,09	32,41	27,23	30,12	26,01	31,35
‹NSe-SpP	8,62	5,27	11,88	7,52	9,79	6,41	10,63
Σ Bjork	387,74	378,96	398,35	385,09	392,87	382,53	396,28
Dental parameters							
Linear parameters (mm)							
Overbite	3,05	0,94	4,17	2,62	3,27	1,57	3,66
Overjet	6,61*	4,49*	8,74*	6,19*	6,98*	5,53*	7,91*
Angular parameters (°)							
‹U1-L1	116,88**	114,17**	119,73**	115,96**	117,52**	115,04**	118,81**

Note: * – reliability of statistical differences at the level of p≤0.05 by the Mann-Whitney criterion in relation to the comparison group; ** - reliability of statistical differences at the level of p≤0.01 by the Mann-Whitney criterion in relation to the comparison group.

Table 4. Linear, index and angular parameters studied at head TRG in lateral projection; patients with distal occlusion accompanied by deep incisive disocclusion (Subgroup 2, main group)

Parameters	Me	Min	Max	Percentiles			
				Q-25	Q-75	Q-10	Q-90
Skeletal parameters							
Linear parameters (mm)							
N-Me	111,81	107,69	116,74	110,54	113,03	109,12	114,13
N-ANS	49,37**	44,96**	56,05**	48,61**	50,58**	47,19**	52,64**
N-Se	71,24	64,51	75,93	69,58	73,41	66,02	74,86
N-Gn	113,09	102,54	124,17	110,76	118,12	108,08	121,26
A*-SnP	49,63*	43,98*	56,51*	48,72*	51,83*	46,85*	54,77*

ANS-Me	63,72	59,18	69,97	62,87	65,01	61,59	67,09
S-Go	72,66	68,14	79,21	71,52	74,48	69,94	76,39
Pg-Go	74,35	66,27	81,28	72,63	76,17	69,04	78,87
Co-Go	56,71	48,94	63,37	54,90	60,08	52,54	61,73
Index parameters (%)							
N-ANS/ANS-Me	77,48	75,97	80,11	77,36	77,80	76,62	78,46
S-Go/N-Me	64,98	63,27	67,85	64,70	65,89	64,09	66,93
Angular parameters (°)							
‹SNB	76,12**	71,93**	78,97**	75,36**	76,81**	73,84**	77,69**
‹SNA	81,14	77,02	88,45	80,11	82,96	78,69	85,93
‹ANB	4,89	2,94	7,31	4,14	5,58	3,77	6,02
‹Go	121,46	115,03	127,71	119,22	123,80	117,94	125,46
‹SN-Pog	77,31	68,26	85,17	75,16	79,72	73,08	83,05
‹Beta	20,65*	16,16*	23,52*	19,49*	21,91*	18,08*	22,32*
‹NSe-MP	28,17	24,88	31,79	27,52	29,84	26,35	30,93
‹NSe-SpP	8,48	5,46	11,61	7,87	10,02	6,74	10,82
Σ Bjork	389,04	380,13	399,59	386,18	393,40	383,72	397,01
Dental parameters							
Linear parameters (mm)							
Overbite	6,75*	4,81*	7,83*	6,13*	7,22*	5,38*	7,60*
Overjet	4,64	2,92	5,78	4,33	5,05	3,77	5,34
Angular parameters (°)							
‹U1-L1	133,15	130,44	137,82	132,06	134,34	131,69	136,53

Note: * – reliability of statistical differences at the level of p≤0.05 by the Mann-Whitney criterion in relation to the comparison group; ** - reliability of statistical differences at the level of p≤0.01 by the Mann-Whitney criterion in relation to the comparison group.

The results of the dental apparatus evaluation in patients with distal occlusion accompanied by sagittal and deep incisive disocclusion (if compared against similar parameters in patients with physiological occlusion), as is seen from the head TRG in the lateral projection, revealed the following features:

– The N-Me, N-Se, Pg-Go linear gnathic and cranial parameters in the groups match the respective age-related reference values. If compared with the comparison group, the mandible branch (Co-Go) by Me in children of the main groups (Subgroups 1 and 2) is longer by 7.63% and 6.64% (unreliable, p≥0.05), the upper jaw (A*-SnP) is longer by 11.73% and 10.09%, respectively (reliably identified, p≤0.05), while the anterior height of the facial skull (N-Gn) was found to be reduced by 9.69% and 9.18%, respectively (unreliable, p≥0.05);

– The facial skull vertical linear parameters in the main group (Subgroups 1 and 2), if compared with the comparison group, by Me, were reduced – the anterior upper face height (N-ANS) – by 9.02% and 6.80% (reliably identified, p≤0.05), the posterior face height (S-Go) – by

5.26% and 0.48%, respectively (unreliable, p≥0.05), whereas the intergroup statistically significant differences (p≤0.05) based on the anterior lower face height (ANS-Me) have not been identified;

- The match between the ratio of the anterior upper, the anterior lower face height (N-ANS/ANS-Me), the posterior face height as well as the total anterior face height (S-Go/N-Me) and the limits of the averaged normative values with no statistically significant differences (p≤0.05) in the groups, points at a relative balance of the facial proportions;

– The value of ‹SNA found to be within the normative range is indicative of the orthognathic face type. A decrease in the ‹SNB by Me, if put against the comparison group, by 8.31% and by 4.46% (Subgroups 1 and 2, respectively) (reliably identified, p≤0.01) means a retrogenic type of face caused by the mandible retroposition, while the distal position of the mandible against the skull base also confirms an increase in ‹ANB by 163,27% and 116.37%, respectively (unreliable, p≥0.05);

– The mandibular angle (Go) values in the main group (Subgroup 1 and 2), in relation to similar values in the comparison group, taken by Me, were lower by 7.18% and 6.27% (unreliable, p≥0.05); the ‹SN-Pog values exceeding (unreliable, p≥0.05) the ‹SNB values, by Me, in Subgroup 1 and 2 of the main group, point at the anterior position of the chin protrusion. A decrease (against the comparison group) in the ‹Beta value by Me in Subgroup 1 by 31.06%, and in Subgroup 2 – by 28.32% (reliably identified, p≤0.05) means a horizontal type of jaw growth with rotation (spatial orientation) according to the anterior type;

– The parameters of the angle determining the position of the upper jaw base plane relative to the skull anterior base length (‹NSe-SpP) in the studied groups correspond to the age reference intervals. The median sum of the Bjork angles and the angle setting the position of the mandible body base plane relative to the length of the anterior skull base (‹NSe-MP), in the main group (Subgroup 1 and 2), in relation to the comparison group, were reduced by 1.44% and 1.11% (unreliable, p≥0.05), as well as by 8.66% and 9.33%, respectively (unreliable, p≥0.05).;

- The protrusion of incisors in the main group (Subgroup 1) can be seen from a statistically significant (p≤0.05) decrease in the incisor angle Me values ‹U1-L1 by 13.82% with an increase in the overjet parameters by 168.70%, and an increase in the incisor overlap depth in Subgroup 2, which makes a significant (p≤0.05) Me increase of overbite parameters by 216.90% if compared with similar values in the comparison group, while there were no significant differences detected in the angle values ‹U1-L1 in Subgroup 2.

Table 5 shows the data obtained through the cephalometric analysis of the head TRG in the lateral projection performed to identify the hyoid bone topography.

Table 5. Linear and angular parameters identifying the hyoid bone topography; cephalometric analysis, head TRG, lateral projection

Parameters, units change	Me	Min	Max	Percentiles			
				Q-25	Q-75	Q-10	Q-90
Patients in the comparison group							
H-S (mm)	101,64	94,17	107,52	98,85	104,49	96,63	105,71
H-C_{III} (mm)	36,08	31,99	39,65	34,37	37,71	33,82	38,96
H-RGn (mm)	41,16	37,54	44,82	39,78	42,55	38,49	43,78
H-MP (mm)	15,03	10,86	18,17	13,35	16,48	12,21	17,13
H-N (mm)	119,88	102,97	131,18	113,02	124,01	108,45	127,26
H-A (mm)	75,94	67,91	84,82	72,03	78,76	70,15	81,49
H-B (mm)	49,26	38,89	58,06	45,12	54,33	42,75	56,09

‹H-Me-MP (°)	18,87	14,33	23,79	17,04	20,92	15,39	22,30
‹HGo-HMe (°)	129,31	119,58	137,66	125,92	133,54	121,71	135,08
Patients of the main group of the 1st subgroup							
H-S (mm)	86,85*	80,63*	94,19*	84,38*	89,16*	83,01*	91,43*
H-CIII (mm)	26,91*	23,97*	29,73*	25,56*	28,04*	25,06*	28,82*
H-RGn (mm)	32,14*	28,98*	35,02*	31,25*	33,01*	30,37*	33,69*
H-MP (mm)	7,88*	5,16*	11,04*	7,09*	8,57*	6,41*	9,49*
H-N (mm)	127,98	110,07	137,13	122,02	131,35	116,84	134,90
H-A (mm)	81,17	68,14	89,08	76,36	84,21	73,01	86,63
H-B (mm)	46,03	29,35	54,09	41,48	49,27	36,67	51,71
‹H-Me-MP (°)	12,27*	8,92*	16,71*	11,13*	13,65*	10,32*	15,09*
‹HGo-HMe (°)	144,23*	133,85*	154,07*	141,39*	147,12*	138,44*	149,92*
Patients of the main group of the 2st subgroup							
H-S (mm)	87,72*	81,18*	93,66*	85,03*	88,97*	83,30*	91,14*
H-CIII (mm)	26,68*	24,21*	29,52*	25,21*	27,90*	24,87*	28,93*
H-RGn (mm)	31,87*	29,27*	34,81*	31,19*	32,95*	30,56*	33,48*
H-MP (mm)	8,23*	5,38*	10,85*	7,34*	8,86*	6,53*	9,37*
H-N (mm)	126,52	108,83	135,97	121,38	130,44	115,90	134,05
H-A (mm)	80,69	67,74	88,43	75,08	83,58	72,12	85,82
H-B (mm)	45,19	28,67	53,01	40,17	48,31	34,94	50,56
‹H-Me-MP (°)	12,76*	9,41*	16,63*	11,47*	13,84*	10,59*	15,22*
‹HGo-HMe (°)	143,59*	134,06*	153,79*	141,52*	147,04*	138,61*	150,11*

Note: * – reliability of statistical differences at the level of $p \leq 0.05$ by the Mann-Whitney criterion in relation to the comparison group.

As the cephalometric analysis of the head TRG (lateral projection) revealed, patients with physiological occlusion, if compared to the main group (Subgroup 1 and 2), featured the predominance of the following parameters relative to the hyoid bone body (H): the distance to the central point of the Turkish saddle (H-S) - by 14.55% and 13.69% (reliably identified, $p \leq 0.05$); the distance to the lower point of the anterior edge of the third cervical vertebra body (H- CIII) - by 25.42% and 26.05% (reliably identified, $p \leq 0.05$); the distance to the posterior point of the chin symphysis (H-RGn) - by 21.91% and 22.57% (reliably identified, $p \leq 0.05$); the distance to the mandible body base plane (H-MR) - by 47.57% and 54.76% (reliably identified, $p \leq 0.05$); the distance to the distally located point on the anterior contour of the mandible apical base (H-B) - by 6.56% and 8.26% (unreliable, $p \geq 0.05$); the angular values of the inclination to the mandible body base plane of the (‹H-Me-MP) – by 34.98% and 32.38% (reliably identified, $p \leq 0.05$).

During that, children with physiological occlusion, if compared with the main group (Subgroup 1 and 2), had a decrease in such indicators as the distance from the hyoid bone body to the anterior point of the nasolabial suture (H-N) – by 6.33% and 5.25% (unreliable, $p \geq 0.05$); the distance from the hyoid bone body to the distal point on the anterior contour of the upper jaw apical base (H-A) - by 6.44% and 5.89% (unreliable, $p \geq 0.05$); the position angle of the hyoid bone body relative to the plane of the lower jaw body base (‹HGo-HMe) - by 10.34% and 9.94% (reliably identified, $p \leq 0.05$).

An assessment of the hyoid bone topography in children diagnosed with distal occlusion, compared with patients featuring physiological occlusions, indicates a statistically significant ($p \leq 0.05$) reduction in the distance between the mandible body and the hyoid bone body, as well

as its retrograde (posterior) position relative to the plane of the mandible body base (upward and posterior displacement of the hyoid bone body) (Fig. 4-6).

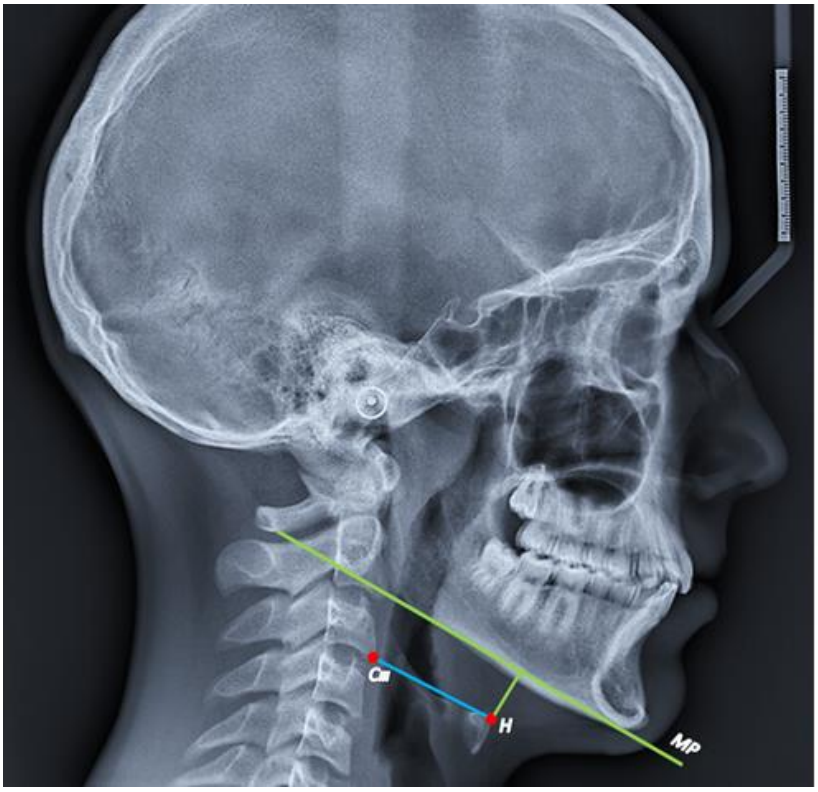

Fig. 4. Linear parameters of H-C_{III} and H-MP on TRG of the head in lateral projection of patient R., 17 years old, with physiologic occlusion.

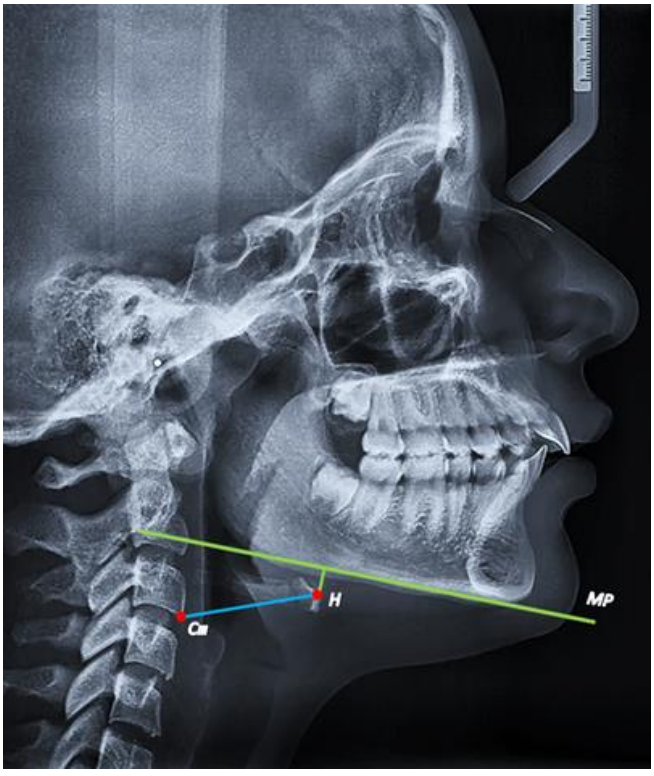

Fig. 5. Linear parameters of H-C_{III} and H-MP on TRG of the head in lateral projection of patient K., 16 years old, with distal occlusion accompanied by sagittal incisal dysocclusion.

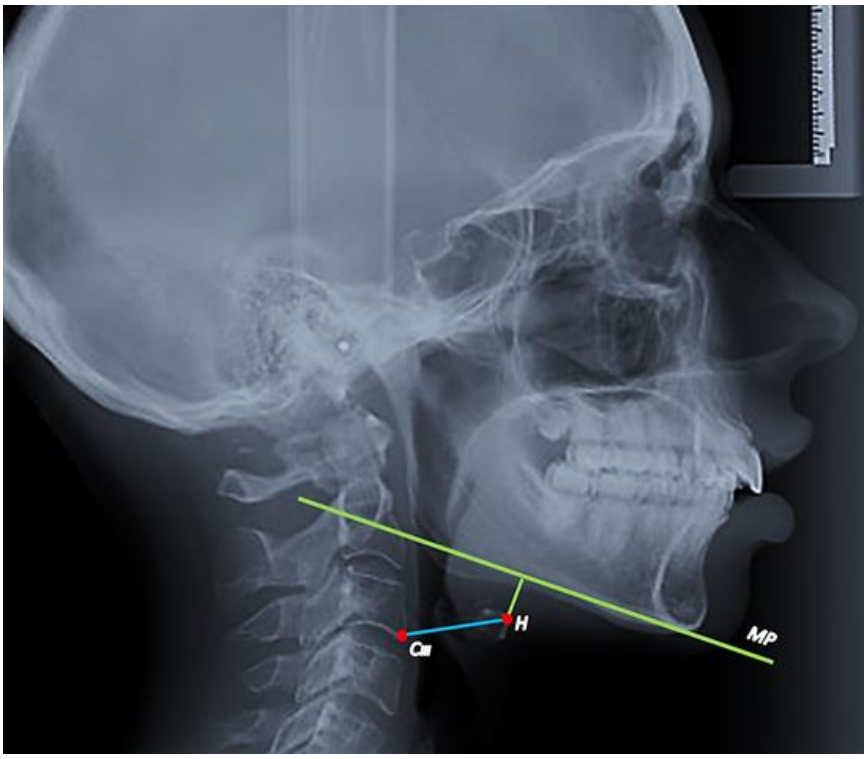

Fig. 6. Linear parameters of H-C_{III} and H-**MP** on head TRG in lateral projection of patient A., 15 years old, with distal occlusion accompanied by deep incisal dysocclusion.

In case of the skeletal distal occlusion (‹ANB exceeding 4º), related to sagittal malocclusion due to inferior retrognathia relative to the skull anterior base or functional insufficiency of the facial and masticatory muscles, a mesial location of the upper jaw, if compared with the lower one, was diagnosed with a significant ($p \leq 0.05$) increase in its length (A*-SnP), as well as displacement of the mandibular body backward (distally) due to decreased parameters ($p \geq 0.05$) of the mandibular angle (Go). A statistically significant ($p \leq 0.05$) shift of the hyoid bone is associated with the mandible movement, both vertically (upward) and horizontally (backward with rotation).

According to the analysis of the hyoid bone topography (H) relative to the tongue, measured by the perpendicular length from its uppermost and anterior point to the C_{III}-**Me** line (Rocabado M., 1984), 94.1% of children (n=32) in the comparison group were found to have the values of the perpendicular length (5.0±2.0 mm) within normative values, while patients of the main group (Subgroup 1 and 2) revealed reference intervals in 80.5% (n=33) and 80.0% (n=28) of cases, respectively.

5. Conclusions

The differentiated values of the linear, index and angular parameters of the head TRG in the lateral projection identified through cephalometric analysis in children aged 15-17 years with distal occlusion allow full assessment the nature of the disturbances affecting the facial skull morphology, as well as the intensity of skeletal pathology. This category of patients features a distal position of the lower jaw in relation to the skull anterior base (‹SNB by Me 73.05°-76.12°; $p \leq 0.01$), an increase in the maxillary angle ‹ANB by Me up to 4.89°-6.95° ($p \geq 0.05$), as well as an

increase in overjet by Me up to 6.61 mm ($p \leq 0.05$) in Class II of Subclass I, and an overbite by Me up to 6.75 mm ($p \leq 0.05$) in Class II of Subclass II.

Clinical and radiological explanation, approbation of the linear (H-S, H-CIII, H-RGn, H-MP, H-N, H-A, H-B) and the angular (‹H-Me-MP, ‹HGo-HMe) informative and diagnostically significant head TRG parameters, obtained while employing craniometric points, allow an objective assessment of the topography of the os hyoideum and its associated structures not in relation to the skull anterior base only (vertical), yet also to the cervical spine (horizontal).

An altered topography of the hyoid bone (H) in patients aged 15-17 years with distal occlusion, accompanied by sagittal and deep incisive disocclusion, can be observed in the vertical and horizontal directions. As could be seen from the cephalometry of the lateral head TRG, the children of the main group (Subgroup 1 and 2), if compared with the patients with physiological occlusion, had the vertical movement of os hyoideum, which was obvious from a significant ($p \leq 0.05$) decrease by Me of H-S linear values – 1.17 and 1.16 times; H-RGn – 1.28 and 1.29 times; H-MP - 1.91 and 1.83 times; the angular H-Me-MP value – 1.54 and 1.48 times; while the horizontal os hyoideum shift serves proof to a significant ($p \leq 0.05$) decrease in the $H\text{-}C_{III}$ distance – 1.34 and 1.35 times with an increase in the HGo-NM angle – 1.16 and 1.11 times, respectively.

The detected upper and posterior displacement of the hyoid bone in patients with gnathic distal occlusion, combined with a decrease in the distance to the mandible plane (body), is one of the key pathogenetic factors behind upper respiratory tract obstruction and nocturnal apnea (Fig. 7-9).

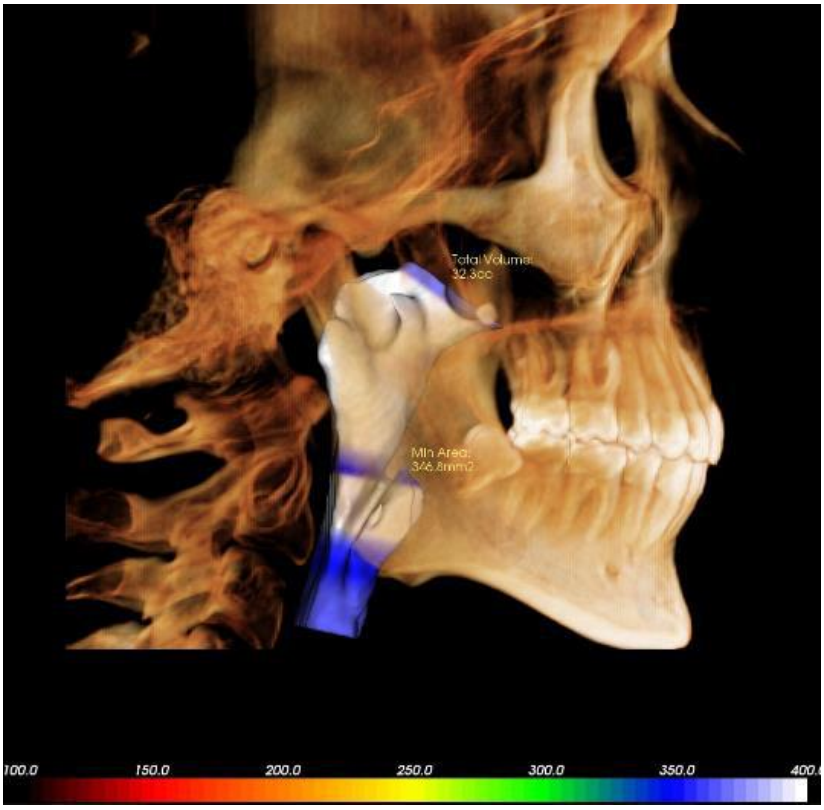

Fig. 7. 3D reconstruction of the upper airway of patient B., 17 years old, with physiologic occlusion. Airway volume is within normal limits.

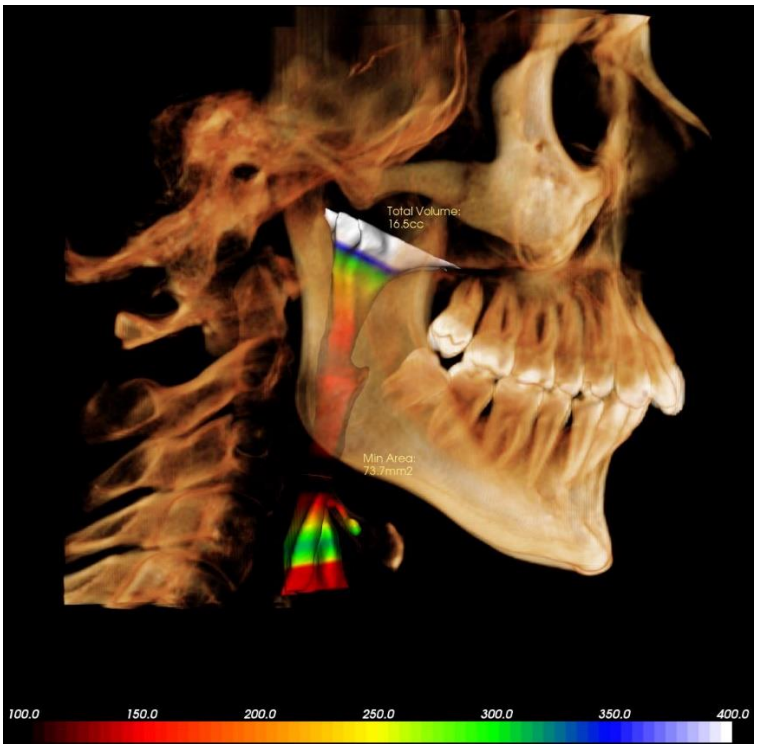

Fig. 8. 3D reconstruction of the upper airway of patient O., 17 years old, with distal occlusion accompanied by sagittal incisal dysocclusion. Airway restriction at the level of C_I - C_{III} vertebrae.

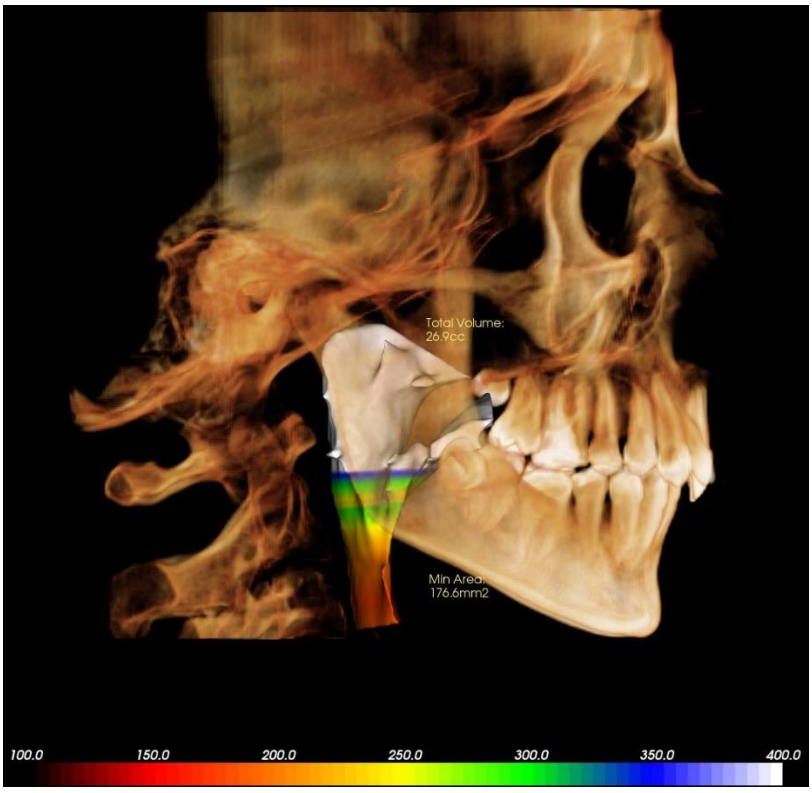

Fig. 9. 3D reconstruction of the upper airway of patient D., 16 years old, with distal occlusion accompanied by deep incisal dysocclusion. Restriction of the airway at the level of the C_{III} vertebrae.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

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Article

Pathogenetic Mechanisms of the Influence of SARS-COV-2 on the Pathology of the Thyroid Gland (Clinical And Experimental Study)

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Abstract:

Abstract: In 2022-2024, the study of the pathogenesis of thyroid diseases is most relevant due to the increased level of stress and the emergence of various early and late consequences of the past COVID-19 pandemic.The purpose of the study is to study the pathogenetic mechanisms of the influence of SARS-COV-2 on the pathology of the thyroid gland in a model experiment on laboratory animals and in statistical studies of the structure of morbidity during the COVID-19 pandemic.

In a model experiment on two species of laboratory rodents sensitive to the SARS-COV-2 virus, the morphology and molecular biology of thyroid tissue was studied using histological and immunohistochemical methods. In the clinical part of the work, a retrospective analysis of the structure of the incidence of surgical pathology of the thyroid gland was performed based on diagnostic results at the preoperative and postoperative stages over 4 years (2019-2023). All quantitative data are processed by statistical methods.Results were obtained indicating that, based on the pathophysiology of SARS-CoV-2 infection, patients with COVID-19 often experience symptoms of thyroid dysfunction, thyroiditis associated with antigenic mimicry of the virus and activation of a three-level regulatory axis, cytokine storm, autosensitization leading to damage to thyrocytes and initiating thyroiditis. These patterns were also revealed in a model experiment on humanized B6.Cg-Tg (K18-ACE2) 2 Prlmn Ifnar1- mice (Stock No. 035041, The Jackson Laboratory, USA) and Syrian hamsters sensitive to the virus. A retrospective analysis over a period of 4 years showed an increase in the number of patients with autoimmune thyroiditis and toxic goiter, an increase in the percentage of nodular formations requiring surgical intervention, with suspected atypia or with reliable signs of cancer (III-VI categories according to Bethesda) from 8.8% to 16 .6%, an increase in the incidence of papillary cancer by 10.3%.

Thus, against the background of immunosuppressive therapy and the general negative impact on the body of severe acute respiratory syndrome caused by this type of coronavirus, it is important to pay close attention to the thyroid gland of patients, an appropriate assessment of low-grade fever and cardiovascular disorders is important, and further fundamental research is advisable to study the long-term consequences of the pandemic on carcinogenesis.

Keywords: thyroid gland, pathological physiology, SARS-CoV-2 virus, autoimmune thyroiditis

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1. Introduction

At present, the study of pathogenetic mechanisms of thyroid gland (thyroid) pathology development has acquired special relevance. In addition to the main risks, such as: man-made disasters and destabilisation of the nuclear power industry, iodine deficiency, the action of stressors in the period of aggravation of geopolitical conflicts, a new factor of pathogenic action has appeared. High incidence of surgical pathology of the thyroid, progressing in 2020-2023 in connection with the pandemic COVID-19 [1]. At the same time, the high incidence of thyroid cancer, including among young people and children, the first place among malignant tumours of the endocrine system, as well as the highest rate of increase in the incidence of thyroid cancer among other types of carcinomas draws attention [2, 3]. The COVID-19 pandemic affected more than 670 million people and its minuscule consequences are still relevant after subsiding. The infection affects the endocrine system, whose dysfunction is caused by: direct damage by the virus to the gland or mediated effects on the regulatory axis, through the effects of systemic inflammation, circulatory disorders, autoimmune reactions due to antigenic mimicry associated with cross-reactivity with thyroperoxidase, sensitisation by adjuvants in vaccination [4]. There are correlations between thyroid dysfunction detected in 15-64% of patients and the clinical severity of COVID-19 [5, 6]. Inflammation of the thyroid and its damage are cytokine-mediated and are accompanied by either an increase in thyroxine production or thyrocyte death [5, 6].

The aim of the study was to investigate the pathogenetic mechanisms of the effect of SARS-COV-2 on thyroid pathology in laboratory animal experiments and in studies of morbidity patterns during the COVID-19 pandemic.

2. Patients and Methods

Morphology and molecular biology of the thyroid tissue were studied in a model experiment on two species of laboratory rodents sensitive to SARS-COV-2 virus (Syrian hamsters and mice of B6.Cg-Tg (K18-ACE2) 2 Prlmn Ifnar1- line (Stock No. 035041, The Jackson Laboratory, USA) using light microsocopy and immunohistochemical method (IHC). The structure of the gland was studied at 5, 10 and 30 days after infection. IHC was performed in a Bond-MAX processor with label detection by Bond Polymer Refine Detection System (Leica, UK). Preparations were scanned on Aperio CS2 (Leica, USA), using Aperio Image Scope at 40x in 5 fields. Lymphocyte differentiation markers CD4, CD8, CD68, CD20, CD138, CD30 as well as cKit, iNOS, Cyclin D1, p16, p63 and MMP3, CD95, Tie2, VEGF were studied. Digital data were processed in STATISTICA 10.0. Me[Q1;Q3] were determined. Differences were determined by Mann-Whintney method by comparison with the intact group. In the clinical part of the work, a retrospective analysis of the structure of morbidity of surgical pathology of the thyroid according to the results of diagnostics at the preoperative and postoperative stages for 4 years (2019-2023) was performed with comparison by chi-square criterion, with $P \leq 5\%$.

3. Results

After intranasal infection of laboratory rodents with virus obtained from a sick person, respiratory infection develops in animals on 2-3 days, for mice high severity of respiratory dysfunction is more characteristic. Clinical recovery occurs on 10-15 days. Morphological and molecular changes in the thyroid tissue develop by the end of the first and beginning of the second week after infection, there is activation of the cell cycle in thyrocytes (increased expression of

markers of mitosis and apoptosis, angiogenesis and extracellular matrix modelling). Signs of inflammation in the tissue - increased expression of macrophages, T-helpers and B-lymphocytes - were also detected. In the recovered animals on the 30th day of the experiment there is still an increase in the number of T- and B- cells compared to the control group (Table 1). These changes are more characteristic for females.

Table 1. Expression level of lymphocyte differentiation markers in control and experimental animals (number of cells in the field of view at 40x magnification, Me[Q1;Q3]).

Group	Intact	Females, 5 days	Males, 5 days old	Females 10 days	Males 10 days old	Females 30 days	Males 30 days old
CD4	2 [1;3]	1 [0;2]#	3 [1;4]	5 [4;5]^	2 [2;3]	5 [4;5]^ *	1 [1;1]
CD138	3 [3;4]	1 [1;2]^	4 [3;4]	1 [1;2]	3 [2;3]	5 [2;3] ^*	3 [2;3]
CD163	4 [1;3]	3 [2;5]	5 [5;6]	7 [6;7]	4 [2;5]	6 [3;3]*	3 [2;3]

* - differences from intact animals

^ - differences between males and females at the same experiment term

\# - differences between experiment terms within the same sex.

Retrospective analysis over a period of 4 years showed an increase in the number of patients with autoimmune thyroiditis and toxic goitre, an increase in the percentage of nodules requiring surgical intervention, with suspected atypia or with reliable signs of cancer (Bethesda categories III-VI) from 8.8% to 16.6%, an increase in the incidence of papillary cancer by 10.3% and the detection of tumours at earlier stages of growth compared to the period of 2019 (Table 2).

Table 2. Results of cytology of aspiration biopsy putunctates and histology of thyroid nodules during different periods of the pandemic.

Group	Distribution (in %) according to Bethesda Thyroid Classification		Proportion of cancer (in %) among all nosologies according to post-pore histology data			Proportion of papillary cancer (in %) among all nosologies according to post-pore histology data
	I-II	III- VI	all patients	men	women	gender-neutral
Before the pandemic.	91,2	8,8	38,7	55,6	36,9	22,6
During the pandemic.	85,9	14,1*	31,0	25,0*	30,6	21,4
After the pandemic.	83,4	16,6*	40,8**	20,0*	42,4**	32,9 *, **

Note: * - significant relative to the group before the pandemic, ** - to the group during the pandemic

4. Discussion

We obtained results indicating that, based on the pathophysiology of SARS-CoV-2 infection in COVID-19 patients, the phenomena of thyroid dysfunction, thyroiditis associated with antigenic mimicry of the virus and activation of the three-level regulatory axis, cytokine storm, and autosensitisation leading to thyrocyte damage and initiating thyroiditis are frequently observed. These patterns were also revealed in a model experiment on humanised B6.Cg-Tg (K18-ACE2) 2 Prlmn Ifnar1- mice and Syrian hamsters susceptible to the virus, and are comparable to the results obtained by other authors [5, 6]. The pandemic is characterised by an increase in patient referrals with primary manifestation of thyroid disease, which is somewhat paradoxical in the context of limited routine interventions. During the pandemic a reversible increase in the number of

operations for toxic goiter and adenomas on the background of gland hyperfunction and irreversible increase in the proportion of malignant tumours was established; predominance of more differentiated forms of cancer with low risk prognosis, as well as tumours at earlier stages, frequent detection of prognostically more favourable forms after the pandemic.

5. Conclusions

Thus, against the background of immunosuppressive therapy and the general negative effect on the organism of severe acute respiratory syndrome caused by coronavirus, it is important to focus on the thyroid of patients, the appropriate assessment of subfebrile and functional disorders is important, and further basic research to study the long-term effects of the pandemic on carcinogenesis in the thyroid tissue is appropriate.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

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Article

CORRELATION of COGNITIVE FUNCTIONS with DENTAL STATUS

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Abstract:

Introduction: Maintaining oral health with age is crucial for healthy longevity, as it is associated with improving the processes of swallowing, chewing, nutrition, communication, and socialization. This is an important indicator of overall health, well-being and quality of life. The poor condition of the oral cavity is characterized by tooth loss and periodontitis. They are widespread among the elderly, especially among people with weakness and cognitive impairment.

The aim of the study was to assess the dental condition of the elderly people included in the study and its relationship with cognitive impairment.

Materials and methods: this scientific study was conducted during 2022-2023 were examined in everyday practice at a dental clinic in Khimki. A total of 40 people aged 60 to 94 years were included in the study (the average age was 72.5±10.06 years), including 19 people with good cognitive status, 21 people with poor cognitive status. The study assessed the geriatric, dental and somatic status of patients. All patients who were diagnosed with cognitive decline were given individual recommendations for the treatment and prevention.

Results: In the course of the study, it was found that there is heterogeneity of geriatric status in patients undergoing dental treatment. It turned out that 19 patients out of 47.5 % have an MMSE test score in the range of 28-30 points, which indicates the absence of cognitive impairment, and 21 patients (52.5%) have less than 28 points, which reveals cognitive impairment. One patient (2.5%) of the total number of examined patients was diagnosed with severe dementia.

Conclusion: the present study showed that patients with dementia had a significant decrease in the hygienic status of the oral cavity, a progressive course of periodontal diseases, as well as significant tooth loss. The problem of impaired dental status in patients with cognitive dysfunctions requires further clinical interdisciplinary research to assess cognitive functions and oral health.

Keywords: oral health, dentistry, cognitive functions, gerodontology, gerontostomatology, geriatrics, dementia

1. Introduction

Maintaining oral health as we age is crucial for healthy longevity as it is associated with improved swallowing, chewing, eating, communication, socialisation. It is an important indicator of overall health, well-being, and quality of life. Poor oral health is characterised by tooth loss and

periodontitis. They are common among older people, especially those with frailty and cognitive impairment.

2. Patients and Methods

This scientific study was conducted during 2022-2023 on the basis of a private dental clinic in Khimki. Khimki. A total of 40 people aged 60 to 94 years (mean age was 72.5±10.06 years), including 19 people with good cognitive status and 21 people with poor cognitive status were included in the study. The geriatric, dental and somatic status of the patients was assessed during the study. Inclusion criteria: elderly age 60-94 years, absence of oncological disease, absence of contraindications to dental treatment.

3. Results

The present study included two phases. Stage 1: comprehensive geriatric assessment of patients subject to dental treatment. Data were extracted from primary medical records, questionnaire survey, instrumental dental examination. Specialised questionnaires and scales were used for this purpose: the Minimental State Examination (MMSE) Brief Mental Status Evaluation Scale and the "Clock Drawing" test. Stage 2: comparative analysis of dental and geriatric status in patients undergoing dental treatment.The study revealed that there is heterogeneity of geriatric status in patients undergoing dental treatment. It was found that 19 patients (47.5%) had MMSE test score between 28-30 points indicating no cognitive impairment and 21 patients (52.5%) had less than 28 points revealing cognitive impairment. One patient (2.5%) of the total number of patients examined was found to have severe dementia. A significant correlation between the number of lost teeth, low level of hygiene, poor periodontal index and the degree of cognitive impairment was revealed. It turned out that people with the number of extracted teeth 3.78±6.32, good and satisfactory oral hygiene, and periodontal index CPITN 1.73±0.87 points have MMSE test score of 25-30 points, which indicates the absence of cognitive impairment. Further increase in the number of lost teeth, poor hygiene and periodontal CPITN index leads to a high probability of development of senile dementia. Thus, among patients who lost an average of 8.41±6.34 teeth, the MMSE test showed a score of 24 - 27, indicating pre-dementia cognitive impairment in these patients. Among those who lost 9.33±4.72 teeth, mild dementia was detected. In patients with MMSE index scores 0-19 the number of extracted teeth ranged from 20±11,89 to 32. In this group of patients dementia manifestations of moderate and severe degree of severity. Meanwhile, the dependence on the level of oral hygiene was also revealed. Patients with good cognitive functions demonstrate sufficient and satisfactory level of hygiene. The index of hygiene index OHI-S corresponds to 1.4±1.47, which is a satisfactory level of hygiene. Patients with a good level of oral hygiene have a low risk of developing dementia. Patients with this level of risk have a high chance of avoiding the development of dementia. With a satisfactory level of oral hygiene, patients need extra attention and may have some chance of developing dementia. Patients with unsatisfactory and poor oral hygiene, have a high risk of developing dementia. Urgent action should be taken to improve oral health in these patients. Periodontal CPITN index in patients with MMSE scores 0-27 averaged a code of 2.88±0.19, indicating the presence of bleeding gums, tartar and pathological gum pockets (Fig. 1).

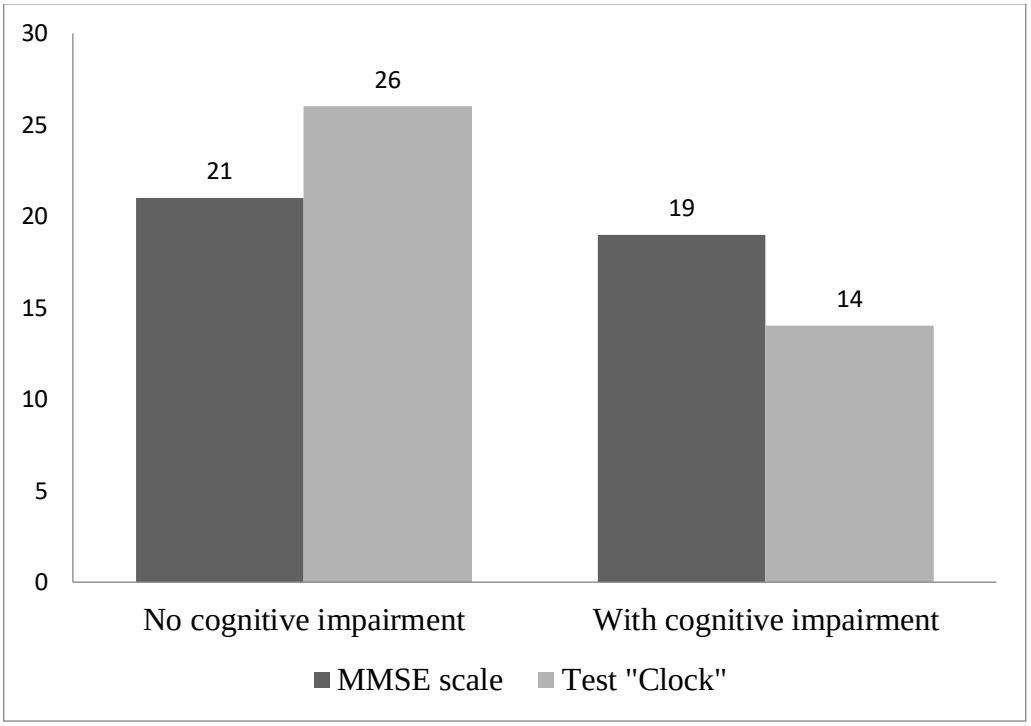

Figure 1. Assessment of cognitive functions of patients using the MMSE scale and the "Clock Drawing" test at the first stage of the study.

4. Discussion

With the decline in cognitive function, the increase in periodontal disease is not surprising, as adequate plaque control and oral care require both cognitive and motor skills. To prevent these problems, it is recommended that patients and their carers be supported and assisted with oral care. Based on the results of the study, a methodology for adapting medical procedures and clinical approaches in patient care is being developed to improve the accessibility of dental care for patients with senile dementia. Knowledge and understanding of a patient's cognitive and mental state can facilitate communication and support dental care. Oral health is both a marker and predictor of cognitive impairment. Oral health is a modifiable risk factor that is often neglected in clinical practice. Standards of clinical practice to guide the management of complex treatment of older people with, personalised targeted therapies in dental practice is a pressing unmet need and the integration of oral health into routine clinical practice and primary care should be a priority for every region. Every physician should identify oral health problems in a timely manner, and dentists should identify cognitive impairment with appropriate treatment. Since oral health and cognitive impairment are modifiable risk factors for healthy ageing, population-level screening for correlations between oral health status and cognitive impairment should be a priority.

5. Conclusions

In the process of this scientific study, it was revealed that elderly and elderly patients who seek oral health care in a dental clinic need not only standard clinical and paraclinical examinations within the framework of dentistry. The present study showed that patients with reduced cognitive functions had a significant decrease in oral hygiene status, progressive course of periodontal diseases, and significantly pronounced tooth loss. The problem of impaired dental

status in patients with cognitive dysfunction requires further clinical interdisciplinary research on the assessment of cognitive function and oral health.

Application of artificial intelligence:

The article is written without the use of artificial intelligence technologies.

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Facial Reanimation with Labbe Myoplasty Followed by Complex Rehabilitation

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Abstract:

Introduction: the tumor's presence in the parotid salivary gland can lead to the development of facial paralysis in 1.67% of cases, and parotidectomy for neoplasms of this localization is complicated by iatrogenic damage to the facial nerve in 6-29.6%. Neurological insufficiency of the facial nerve leads to poor health state, both physical and mental. The facial resuscitation which includes a complex of therapeutic and surgical, together with rehabilitation measures, reduce these complications and improve the general condition of the patient. Lengthening temporalis myoplasty according to Labbé is recommended for use in facial nerve paralysis of various etiologies, including posttraumatic (iatrogenic) paralysis. This article describes the first case of facial reanimation by Labbe temporal lengthening myoplasty performed in the department of head and neck tumors of Voronezh Regional Clinical Oncological Dispensary with subsequent complex rehabilitation.

Case: patient Ch., 52 years old (WAS born. in 1972), was diagnosed with: Cancer of the right parotid salivary gland, stage II T2N0M0, after combined treatment. Histologic diagnosis: adenocystic carcinoma. In 2021, the patient underwent combined treatment, the surgical component of which included parotidectomy with fascial-futlar excision of the neck fiber. The paralysis of the facial muscles appeared after the operation. After two years, the patient turned to the specialists of the head and neck tumor department of VRCOD with complaints of lacrimation from the right eye, its dryness and salivation on the right side. It was decided to perform myoplasty by lengthening the temporal muscle. After 3 months of complex rehabilitation, patient C. has complete eyelid closure on the affected side of the face, almost complete symmetry of the corners of the mouth, absence of lacrimation, salivation and "sail symptom" on the right side. She has already mastered the temporomandibular smile and has begun to learn the voluntary temporal smile. Rehabilitation continues as planned.

Conclusively: the first precedent of Labbe myoplastyapplication in the department of head and neck tumors of Voronezh Regional Clinical Oncologic Dispensarywith subsequent complex rehabilitation can be considered successful. The further use of this technique will be advisable with the possibility of gradual introduction into practice more methods of surgical facial resuscitation and improvement of the developed rehabilitation tactics.

Keywords: clinical case, oncology, facial resuscitation, complex rehabilitation

1. Introduction

The incidence rate of major salivary gland cancer remains stable with no downward trend, and the proportion of this group of pathologies among all malignant tumors of the head and neck ranges from 3 to 6% [1-4]. The tumor most often develops in the parotid salivary gland (in 90%) [2]. That one of the key clinical manifestations of this group of neoplasms in the development of locally spreading process is the lesion of n. facialis [1,5]. The tumor's presence in the parotid salivary gland can lead to facial paralysis in 1.67% of cases [6], and parotidectomy for cancer of this localization is complicated by iatrogenic damage to the facial nerve in 6-29.6% [7,8].

Neurological insufficiency of the facial nerve leads to poor health state, both physical and mental [6,9,10].

The facial resuscitation which includes a complex of therapeutic and surgical, together with rehabilitation measures, reduce these complications and improve the general condition of the patient. The surgical group of techniques includes temporal lengthening myoplasty according to the Labbe method, recommended for use in facial nerve paralysis of various etiologies, including posttraumatic (iatrogenic) [11-14].

This article describes the first case of facial resuscitation by Labbe temporal lengthening myoplasty performed in the department of head and neck tumors of the Voronezh Regional Clinical Oncological Dispensary (VRCOD) with subsequent complex rehabilitation.

2. **Presentation of a clinical case**

Patient Ch., 52 years old (WAS born. in 1972), was diagnosed with: Cancer of the right parotid salivary gland, stage II T2N0M0, after combined treatment. Histologic diagnosis: adenocystic carcinoma. In 2021, the patient underwent combined treatment, the surgical component of which included parotidectomy with fascial-futlar excision of the neck fiber. The paralysis of the facial muscles appeared after the operation.

After two years, the patient came to the specialists of the Head and Neck Tumor Department of VRCOD with complaints of lacrimation from the right eye, its dryness and salivation on the right side. At the initial examination in the hospital: on the affected side of the face, smoothing of skin folds, swelling of the cheek ("sail symptom") when exhaling and talking, lagophthalmos. No other features were detected during physical examination.

Taking into account the fact that the absence of functional load on mimic muscles for 2 or more years leads to the complete loss of their ability to contract due to fiber atrophy and its replacement by connective tissue [15], we decided to perform myoplasty by lengthening the temporalis muscle. The existing lagophthalmos was treated with blevarorrhaphy aimed at achieving permanent narrowing of the eye slit on the side affected by paralysis. The early postoperative period proceeded without complications (except posttraumatic edema).

The rehabilitation process was divided into two periods: early (3-4 weeks after surgery) and late (1 month after surgery). The first period is characterized by the most gentle attitude to the tissues of the postoperative area. Excluded significant loads on mimic and masticatory muscles, methods of physiotherapeutic influence are not used. Also, taking into account the traumatic nature of the operation and the presence of a pronounced postoperative edema on the face, already in the early postoperative period (2 times a week and as needed) with the patient began to work staff psychologist VRCOD to provide professional psychological support and motivation for further rehabilitation. The work with the psychologist continued throughout the entire period of hospitalization.

The second period includes a number of measures aimed at compensating for the previously lost functions. Physiotherapeutic treatment is used, but an important feature of working with cancer patients is that the impact should not be applied to the area where the tumor focus was previously located, so as not to provoke the progression of the disease. The following methods are used: acupuncture (3 months) - once a week; therapeutic facial massage (self-massage) (the whole rehabilitation period) - 5-7 minutes twice a day; therapeutic gymnastics (complex of mimicry exercises) (the whole rehabilitation period) - 15 minutes 5 times a day independently, as well as once a week visit to a speech therapist. Much attention is paid to the development of the smile, the author of described methodology emphasized 3 stages [14]: 1st - temporomandibular smile (clenching teeth to smile), 2nd - voluntary temporal smile (thinking about the contraction of temporal muscle, not clenching teeth when smiling), 3rd - spontaneous smile (facial expression changes on demand, in imitation or depending on the situation). In addition to sessions with a physiotherapist and speech therapist, the patient continues to work with a psychologist (1-2 times a month and as needed).

After 3 months of comprehensive rehabilitation, patient Ch. has complete eyelid closure on the affected side of the face, almost complete symmetry of the corners of the mouth, no lacrimation, no salivation and no "sail symptom" on the right side. She has already mastered the temporomandibular smile and has begun to learn the voluntary temporal smile. Rehabilitation continues as planned (Fig. 1).

Figure 1. The result of treatment and rehabilitation (before surgery (a) and 93rd day after surgery (b))

3. Conclusions

The clinical case clearly demonstrates the need to introduce such reconstructive manipulations into the list of services of medical institutions working in the field of head and neck tumors. Their application will maximally compensate for the neurological deficit arising as a consequence of the underlying disease itself or as a complication of surgical removal of the neoplasm. Therefore, the first precedent of Labbe myoplastyapplication in the department of head and neck tumors of Voronezh Regional Clinical Oncologic Dispensarywith subsequent complex rehabilitation can be considered successful. The further use of this technique will be advisable with the possibility of gradual introduction into practice more methods of surgical facial resuscitation and improvement of the developed rehabilitation tactics.

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