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Improving The Results Of Treatment Of Locally Advanced Oropharyngeal Cancer With The Study Of Epidemiological And Molecular Biological Features (Literature review)

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ABSTRACT

To provide data on improving the results of treatment of locally advanced oropharyngeal cancer, taking into account epidemiological and molecular biological characteristics.

Keywords:

Malignant neoplasms, oropharyngeal cancer, oral cavity, oropharynx

Introduction. Oral cancer (RR) is a serious public health problem, with more than 200,000 new cases reported worldwide each year, 2/3 of which occur in developing countries. The overall mortality rate from RPR remains high and is about 50% even with modern methods of diagnosis and treatment, medical care, which is probably due to the late stage of the disease when it manifests. This review presents recent advances in understanding the significance of the main risk factors for the development of RPR obtained from literature sources, in particular tobacco, alcohol and betel, as well as genetic polymorphisms that determine their metabolism, which may predispose patients to oral carcinoma, viral theory of development

(human papilloma virus (HPV)), in which there are lesions of the epithelium of the oral cavity with the presence of malignant potential.

Oral cancer (RPR), its symptoms and signs have been observed and described by medicine since ancient times. The first descriptions of oral neoplasms were made by prominent doctors and surgeons of ancient civilizations. RPR includes lip cancer and all subtypes of the oral cavity and oropharynx [1]. According to the Globocan researcher, RPR ranks 16th in prevalence and 15th in mortality worldwide, while the incidence of RPR (adjusted for age) in the world is 4.00/000, but it should be noted that its variability is quite significant, which depends on gender, age, country of residence, race and ethnicity

belonging, as well as socio-economic conditions [3]. As it is known, territorial dependencies play an important role in the burden of malignant neoplasms (ZN), and the existing differences between developing and Western countries are undeniable. They are related to the different habits of the population, life expectancy, preventive education and the quality of medical care in each individual country. Thus, in most developing countries, the main factors are poverty, illiteracy, which causes advanced stages of the disease, lack of access to medical care and insufficiently coordinated infrastructure to ensure full-fledged diagnosis and treatment [4]. Many physical conditions, environmental and genetic factors have been identified as a risk of developing RPR [2].

Thus, while in North America and Europe, "high-risk" human papillomavirus (HPV) infections are responsible for an increasing percentage of oropharyngeal cancer among young people, for other infectious agents this relationship is still being discussed (for example, it has been reported that various species belonging to the genus *Candida* produce endogenous nitrosamines from food nitrites present in the oral cavity, especially in saliva) [6]. The mortality rate from it remains high, primarily depending on the stage of the disease at the time of diagnosis, which is often already neglected.

Oral cancer (RPR) is a malignant neoplasm (ZN) that can affect various parts of the mouth and oropharynx, including lips, tongue, cheeks, bottom of the mouth, palate and tonsils. Historically, its symptoms and signs have been observed and described since ancient times. RPR develops in a certain anatomical zone, starting from the lips within the circular area behind, covering the grooved papillae on the back of the tongue, the frontal palatine arches to their junction with the hard and soft palate. In most cases (85-95%), RPR is represented by squamous cell carcinoma [7]. Of the total component of all ZN, 2% is accounted for by RPR per year, due to the high frequency and high mortality rate, this pathology is a serious problem in most countries of the world [8]. After squamous cell carcinomas, tumor variants are carcinomas of the small salivary

glands, such as mucoepidermoid and adenoid cystic carcinomas, basal cell carcinomas, mesenchymal ZN, hematological tumors and melanomas. RPR can develop both independently and from precancerous dysplastic lesions, which manifest themselves in the form of erythroplakia, leukoplakia, submucous fibrosis and lichen planus, as well as their combinations. In these cases, repeated exposure to carcinogens – alcohol, tobacco, a diet low in vegetables and fruits, excessive levels of solar insolation, the presence of HPV viruses contribute to malignant transformation. Squamous cell carcinomas can occur in the form of verrucous or basaloid ZN, which have a poor prognosis. The classification of RPR is based on the definition of histopathological subtypes – keratinization, cellular atypia, nuclear polymorphism, mitotic activity, these processes eventually lead to the division of tumors into well, moderately or poorly differentiated forms. According to retrospective studies [9], it was determined that the bottom - 22% of all cases, as well as the anterior part of the base of the PR (21%) are the most common places of occurrence of RPR, followed by the alveolar process (18%) and the edge of the tongue (15%). The hard palate is identified as a frequent anatomical area of the upper jaw (5%). Thus, the development of RPR involves deep penetration into local structures, with spread to the lymph nodes of the neck and further distant metastasis.

In the early stages of the tumor process and development, no specific symptoms are noted, which causes a lack of attention to the initial stages of the disease among patients, i.e. patients do not turn anywhere until the tumor growth becomes noticeable and causes functional disorders, which explains the fact that up to 50% of RPR are diagnosed on IV and less than 25% in the first stage of the disease.

As for mortality, 188,438 people die annually from this pathology, while the cumulative standardized age indicator is 2.00/000, which means a 50% risk of death with the development of RPR. Of the cumulative number of deaths, men - 122,442 (70.0%), women - 52,473 (29.9%), the age standardization of which is 2.80/000 for men,

1.20/000 for women. It should be noted that the increase in mortality corresponds to aging in both sexes from 0,03-0,050/000 up to 25 years old and 7,9-14,40/000 after 75 years and older.

The distribution of mortality around the world is homogeneous in comparison with morbidity, the highest level is recorded in Asia – 2.4 per 100 thousand population; the average in Europe – 1.7; Oceania – 1.6; Africa – 1.2 and South America – 1.0; significantly low in North America – 0.7. These figures can be correlated directly with the risk of mortality – 70% in Africa, 60% in Asia, 40% in South America and Europe, 20% in North America and Oceania. It should be noted that the mortality from RPR, as well as the incidence in Asia, continues to increase, and over the past 30 years has increased by 1.71 times, compared to other continents where it had stable indicators.

The RPR also occupies a significant place in the structure of the ZN in the Republic of Uzbekistan. According to available statistics, in 2022, 21,976 new cases of ZN were recorded in the Republic of Uzbekistan, 552 of them with RPR, which is 2.51% of the total number. Among the patients with RPR, men accounted for 63.9%, and women - 36.1%, which indicates the predominance of the male sex in the group of patients with RPR as a whole [10]. In the period 2011-2020, 5,015 cases of RPR were registered, of which 3,135 (62.5%) were men and 1,880 (37.5%) were women.

As well as global data, there are regional and territorial differences in statistical indicators of morbidity and mortality, the causal factors and risk of which require in-depth epidemiological study, which is carried out within the framework of this study, described in subsequent chapters.

Risk factors for oral cancer

Among the generally recognized four main risk signs for mortality from RPR, according to the Global Burden of Disease, Injury and Risk Factors Study [11], alcohol consumption and smoking are the most common among men (more than 80%), chewing tobacco - among women (more than 50%). In most cases, RPR is diagnosed among older men, but recent trends show a different picture –

more and more young non-smoking women are exposed to this pathology [12].

Based on known facts, RPR is registered 5-9 times more often in smokers, compared with non-smokers, and the incidence increases 17 times more often among people who smoke more than 80 cigarettes a day [13].

Excessive alcohol consumption increases the negative effects of nicotine, in which the risk of RPR increases by 30 times, among people who consume more than 100 grams per day, with less consumption, the risk increases by 3-9 times [14].

The use of tobacco in the form of chewing, snuffing, as well as electronic cigarettes contributes to the development of RPR, because in this method, catechum nuts or tobacco are used, which is mixed with slaked lime, betel, sweeteners or spices, and they are known to have carcinogenic effects [12].

Ultraviolet insolation of sunlight is also one of the risk factors for developing lip cancer, etc. [16]. Non-compliance with hygiene standards is also one of the factors leading to the development of RPR.

To date, the viral theory of the development of RPR is known, while HPV-16 and 18 types are considered risk factors for the development of the disease, HPV-16 type – in 14.9% of cases, HPV-18 type – in 5.9% [1], HPV-16 type is considered as one of the factors that cause the development of RPR in 3% of cases.

There is a widespread opinion that the difficulty in diagnosing RPR is caused by insufficient awareness of the population about the signs, symptoms and risk factors of this disease [6], which leads to delayed diagnosis and the inability to use conventional clinical research methods.

In 1830, Sir Edward Home published the first article describing human malignant tumors at the microscopic level, followed by explanations by Johannes Muller in 1838 [2]. It was only in the 19th century that histological technology became widespread, and the method of filling samples with wax became a standard technique for preserving biological material for histological studies. In the 21st century, freezing slices has become a common practice.

French botanist Francois-Vincent Raspail was the first to discover the chemical process using microscopic analysis of tissues and cells [9].

The development of technology has contributed to innovative advances, thanks to which significant changes have occurred and knowledge about the possibility of emerging genetic abnormalities, as well as the existence of various types of malignant tumors, has significantly expanded. Over the past 20 years, molecular diagnostic methods have been widely used in clinical practice, significant progress has been achieved using methods of computational cytology, telescope, confocal microscopy, determination of tumor markers, microchipping and other technologies. As is known [12], the lack of modern equipment for working with human tissues has led to a slowdown in the development of surgical pathology. Until the 19th century, according to historical manuscripts, the technique of filling tissue samples with wax was rare, and it was only by the beginning of the 20th century that frozen tissue sections began to be used for morphological research methods []. Potential malignant diseases are quite difficult to identify during a standard clinical examination, and therefore microscopic studies of damaged cells and tissues are the basis for the diagnosis of these conditions [4]. The lack of resources for the prevention and treatment of RPR has led to the fact that there is currently a tendency for these diseases to increase, accounting for 50-60% of the majority of lesions in this area [5]. Despite the improvement in the 5-year survival rate from these diseases, it remains low and is no more than 53-60% [11]. The majority of HPV are registered in the late stages of the disease, being one of the main reasons for the insignificant progress in survival rates [7]. The main method included in the diagnosis of RPR is an examination of the oral cavity, which is used to screen patients for diseases and precancerous lesions. Studies of unique genetic profiles that determine pathological processes have acquired great importance in the diagnosis of hereditary diseases and cancers. Understanding standards, as well as other natural cycles assessed by subatomic design, are

key to effective planning and implementation of modern diagnostic methods together with traditional ones.

DNA and RNA molecules are found in the nucleus of every cell in the body. For medical research, DNA is most often obtained from blood, bone marrow and tissue samples taken through biopsy or surgery. Additionally, it is possible to use smears from the inner surface of the cheek. DNA can also be isolated from tissues fixed with formalin and filled with paraffin. The process of their extraction can be carried out from tissues only after the destruction of protein crosslinking, dewaxing and proteinase treatment [6]. Degraded DNA from fixed tissues can be amplified using PCR. At the same time, it is reported that the isolation of RNA from formalin-fixed samples is less effective than from fresh tissues [14].

Conclusions: Thus, with the help of antigens and antibodies, IHC analysis and other modern molecular studies are carried out. The main factor in the timeliness of diagnosis is early access to a specialist: the loss of time in the initial stages of RPR is usually associated with a misunderstanding of the patient's manifestations of the disease, their symptoms, the emergence of a stage of denial and ignoring. The second loss is often associated with insufficient qualifications of medical personnel, dentists, which also aggravates the state of the process. Another loss of time is considered to be the period when the disease is detected and treatment is started. This determines the need to raise public awareness, with training in self-examination programs, as well as professional development of medical workers who provide care to this category of patients.

Literature:

1. Bulgakova N.N., Volkov E.A., Pozdnyakova T.I. Autofluorescence stomatoscopy as a method of oncoscreening of diseases of the oral mucosa // Russian Dental Journal. 2015. Vol. 19, No. 1. pp. 27-30
2. Butenko Z.A., Filchenkov A.A. Modern concepts of viral oncogenesis: fundamental and applied aspects //

- Experimental oncology - 2010. - No. 2. - pp. 239-245
3. Gazhva S.I., Stepanyan T.B., Goryacheva T.P. The prevalence of dental diseases of the oral mucosa and their diagnosis // International Journal of Applied and Fundamental Research. 2014. No.5. pp. 41-44.
 4. Gafur-Akhunov M.A., Yuldasheva D.J. Dynamics of morbidity and mortality from malignant diseases in Tashkent. - /Eurasian Journal of Oncology, 2018, vol.6, No. 1, pp.82-88.
 5. Gevorkov A.R., Boyko A.V., Chernichenko A.V. Targeted modification in radiation treatment of squamous cell carcinoma of the oropharyngeal zone. Bulletin of the RNCRR. 2012. No. 2 (3). p. 171.
 6. Gelfand M.I. The expediency of using induction chemotherapy in the treatment of oral mucosal cancer with the prevalence of the ct2n0m0 process, 2017
 7. Gerstein E.S., Shcherbakov A.M., Obusheva M.N., Kushlinsky N.E. Enzyme immunoassay of vascular endothelial growth factor (VEGF) in tumors and blood serum// Kremlin medicine.-2005.- No.3.- pp.45-52.
 8. Maksimenko P.T., Skripnikova T.P., Khmilte A. Nomenclature, Clinical classification of diseases, changes in the mucous membrane of the oral cavity, lips and tongue // Ukrainian Dental Almanac, 2008 No.4, pp.28-35
 9. Merabishvili V.M. Oncological statistics: (traditional methods, new information technologies) / V. M. Merabishvili. - St. Petersburg: Costa. Part 2. - 2011. - 247 p
 10. Mudunov A.M. A new generation of multitargeted tyrosine kinase inhibitors in the treatment of radiorefract differentiated thyroid cancer, 2015
 10. Mudunov A.M. Surgical treatment of locally advanced recurrent cancer of the oropharyngeal zone. A case from practice, 2013
 11. Paches A. I. Cancer of the oral mucosa. In the book: Tumors of the head and neck. M.: Medicine, 2000. pp.142-155.
 12. Paches A. I., "Tumors of the head and neck" 2013, pp.119.
 13. Written V.I., Written I.V. "Method of reconstruction of the tongue after its half resection", 2016.
 14. Pishny V.I., Kulakova N.M., Pishny I.V. Speech therapy after surgical treatment of malignant tumors of the oropharyngeal zone. // Proceedings of the Samara Scientific Center of the Russian Academy of Sciences, vol. 17, №2(3), 2015, Conference "Modern problems of oncology and hematology" 22-24.04. 2015 Samara. pp.622-627