

Saliva crystallography in patients receiving chemoradiotherapy in virtue of head and neck tumors results

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Abstract

Radiation therapy, chemotherapy or surgery is recommended for early treatment of head and neck cancers according to current standards. Radiation and chemoradiation therapy of head and neck tumors leads to the development of acute and chronic radiation complications in the oral cavity.

Objective: to conduct a qualitative assessment of saliva by crystallography in patients receiving chemoradiation therapy for head and neck neoplasms.

In the period from 2020 to 2021, 50 patients with oral mucositis of varying severity were examined, who received antitumor treatment at the Russian Scientific Center for Roentgenoradiology (RSCRR). Separation of patients: in the I group, dental support was carried out in the form of correcting the skills of individual oral hygiene. In the II group were used prolonged-action herbal preparations toothpaste based. The results were evaluated using saliva crystallography and oral hygiene.

The obtained results of saliva crystallography prove the effectiveness of the use of prolonged-action herbal preparations in patients with oral mucositis of varying severity, receiving chemoradiation therapy.

The advantage of morphological analysis of salivary facies is simplicity, non-invasiveness and is an inexpensive way to assess the health of the oral cavity.

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Introduction

For the head and neck malignant neoplasms treatment the radiation therapy (IMRT, IGRT), chemotherapy or surgical interventions are recommended at the early stages, according to modern standards. For the late one's is recommended the combined therapy. All these approaches to treatment can lead to recovery

and increase the survival rate of cancer patients at this category¹.

Head and neck tumors radiation and chemoradiotherapy leads to the development of acute and chronic complications in the oral cavity, such as radiation caries, radiation gingivitis, mucositis, candidiasis, dysgeusia, xerostomia, osteoradionecrosis, etc.,²⁻⁴. One's complications could lead to the main treatment course interruption and worsens the disease prognosis and increases the hospitalization duration. Besides radiation therapy provide the oral mucosa damage and pronounced functional changes. So it has negative effect on the patients life quality. Thus accompanying therapy programs are becoming particularly relevant, so stress the importance of the dental and oral

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cavity management during chemoradiotherapy of patients^{5,6}.

The head and neck malignant neoplasms treatment complications issues: the occurrence, prevention and treatment should be considered and studied on the basis of an interdisciplinary approach⁷. So it is necessary to determine the various specialists especially dentist roles in the such patients treatment. Due to the timely and effective treatment of chemoradiotherapy oral complications a continuous full course is possible. It should qualitatively improve the effectiveness of treatment⁸.

The cancer patients big number have an oral cavity unsatisfactory condition before the main diagnosis is made, which leads to an increased risk of oral complications. There is also a negative feedback – an oral cavity unsatisfactory condition increases the risk of developing oncological diseases^{9,10}. Thus an important role in the treatment is played by the observance of oral hygiene, which consists in daily care and antiseptic treatment of the oral cavity, which significantly reduces the risk of acute oral complications¹¹.

The main diseases features and the antitumor treatment side effects such as: the risk of infection, low regenerative ability of the mucous, decreased microcirculation, bad general patients' condition make it difficult to conduct clinical and laboratory studies in the oral cavity^{2,12}. So the new approaches to the prevention and treatment of dental complication search and new minimally invasive, but objective methods of confirming the effectiveness of the treatment, continues to be an urgent scientific and clinical task. In this regard, saliva studies are of particular relevance, according to Saibaba, G. et al., 2017, due to their non-invasive and informative nature^{13,14}.

According to Srousi, H. Y. et al., 2017, patients receiving chemoradiotherapy in the head and neck area often suffer from xerostomia. The rate of salivation is significantly reduced in almost all patients¹⁵. According to Porter S. R., et al., 2010, the flow rate of non-stimulated saliva decreases to 60% of the norm. The pH changes to the acidic side with an increase in the sodium content at the background of salivation decreasing. It is known that the protein concentration in saliva increases during radiation and returns to the baseline values before treatment after stopping radiation. Thus, saliva

analysis is a useful diagnostic method for determining the condition of the oral cavity.

Saliva analysis can also be considered as dental therapy adequacy monitoring¹⁶. Recently, a new diagnostic method has been actively developing – crystallography of biological fluids, including saliva. Crystallography is based on the study of the shape, size, color and other characteristics of crystals of the facies of a biological fluid. The basis of the crystallography method is the gradual distribution of substances from saliva as a drop of it dehydrates¹⁷.

The saliva facies crystallography method was chosen for evaluation the dental support clinical results for patients receiving chemoradiotherapy in virtue of head and neck tumors in this study. According to Zhirnova V. A., Vladimirova Yu. V. 2018, studies one's method has sufficient effectiveness in the oral cavity diseases diagnosis¹⁸.

Objective: to evaluate the effectiveness of modern dental support using toothpaste based on mallow, betaine, xylitol and collagen plates with arnica, mint and sodium alginate, aimed at eliminating the oral mucosa mucositis manifestations using the method of saliva crystallography in patients receiving chemoradiotherapy.

Materials and methods

50 patients with oral mucositis of various severity receiving antitumoral treatment in the Russian Scientific Center of Rentgenoradiology were examined in the period from 2020 to 2021. The patients average age was 45±5.8 years. The patients's division was by sex and tumors location. By sex: men - 76.6 % women - 23.4%. By the tumors localization: oropharynx (13.3%), larynx (20%), oral cavity floor (13.3%), larynx (6.6%), nasopharynx (6.6%), maxillary sinus (6.6%), nasal cavity (6.6%), tongue (13.3%), tonsils (13.3%). Most of the tumors detected for the first time corresponded to the III or IV stages of the disease. Of the 50 patients, 24 received combined therapy (chemo-and radiation therapy), 26 received only chemotherapy.

The patients division: in group I, dental support was carried out in the form of individual oral hygiene skills correction, selection of individual oral hygiene products and training of patients in oral care techniques, antiseptic rinses 4-6 times a day - antiseptic solutions of 0.01%

Miramistin solution, 0.02% Furacilin solution, 0.05% Chlorhexidine solution were used; Oleotherapy (applications of vegetable oils (castor, olive, linseed) after a radiation treatment session. In group II, the plant-based prolonged-acting drugs were used: after careful individual oral hygiene a toothpaste based on sodium salt of pyrrolidone carboxylic acid, xylitol, betaine and mallow, the application of collagen plates with chamomile extract, valerian, arnica, mint, sodium alginate, collagenase, collagen №2 - 2 times a day for 3-4 hours, so that the total effect on the mucous membrane during the day was more than 6 hours.

The results were evaluated at the clinical stage (determination of the oral cavity hygienic status, the oral mucositis severity according to RTOG) and at the laboratory stage by saliva crystallography.

The hygienic status of the oral cavity was determined using the Silnes and Loe hygiene index, before and after antitumor treatment.

The oral mucositis severity determination was carried out before and after antitumor treatment, at the stages of 10, 20, 30, 40, 50, 60 Gray by RTOG scale.

Saliva crystallography was performed: each patient was given sterile tubes of 2 ml. The collection of biological material (saliva) in the volume of 1 ml was carried out by patients at 07:00 am, on an empty stomach, before brushing teeth and rinsing the oral cavity, as follows: the patient tilts his head, and without stimulating the salivary glands, collects the saliva that has accumulated in oral vestibule.

Saliva samples were taken three times per day: 1) before chemoradiotherapy or radiation therapy; 2) at the oral mucositis manifestations during chemoradiotherapy or radiation therapy; 3) after treatment completion and oral mucositis symptoms relief.

Preparations for microanalysis were prepared by applying 0.02 ml of saliva to a slide, which were covered with a cover glass, without pressing, so that the saliva was distributed all over the surface of the glass. After that, the glass was dried in a horizontal position at room temperature +18...+25, for 24 hours. Then saliva facies microscopy was performed. The facies of the crystallograms were studied using a Biomed microscope (Russia) at a magnification of 40-100 times.

Criteria for excluding patients from the

study: smoking, surgical interventions in the area of large and small salivary glands, taking drugs that affect the function of the salivary glands.

Results

The hygienic status examination obtained results are presented in (Table 1).

	Silness and Loe Index Indicators	
	I (n=48) M, δ	II (n=42) M, δ
Before dental and oral cavity management	2.48±0.28	2.56±0.21
After dental and oral cavity management	1.7±0.15	1.67±0.09

Table 1. The values of the Silness and Loe index in all groups while determining the hygienic dental status before and after the anti-tumor treatment.

The Silness and Loe indexes are decreasing in both groups. It indicates an improvement in the level of individual oral hygiene.

The oral mucositis signs severity was assessed with the RTOG scale for changes in the oral mucosa during systematic dental examinations at total boost dose 0 Gray (before the start of radiation therapy), 10 Gray, 20 Gray, 30 Gray, 40 Gray, 50 Gray, 60 Gray, and after antitumor treatment in all patients. According to Avanesov A.M. et al., 2019, for patients undergoing chemoradiotherapy for oncological diseases of various degrees localized in the head – neck region, oral mucositis clinical signs begin to appear in 7 days after the therapy start and RTOG is 1.5 immediately, and 3 weeks after the therapy start - RTOG is 3¹⁹. According to Lutsevich O. E. et al., 2015, the RTOG scale is a very subjective assessment method and the introduction of other methods for assessing the severity of side effects of chemoradiotherapy is required²⁰.

The oral mucositis severity dynamic determination obtained results are presented in (Table 2). All patients have the oral mucositis signs increases depending on the total radiation dose. In patients using plant-based prolonged-acting drugs, there was an improvement in indicators. The oral mucositis clinical manifestations in this group are noted with the total boost dose of 16-20 Gray ($p < 0.01$).

Total focal dose	I (n=48) M, δ	II (n=42) M, δ
0 Gray	0	0
10 Gray	0.26±0.06	0.1±0.05
20 Gray	0.44±0.06	0.2±0.02
30 Gray	1.06±0.09	0.6±0.08
40 Gray	1.88±0.03	0.9±0.08
50 Gray	1.9±0.13	1.1±0.09
50 Gray	2.19±0.13	1.5±0.04
One week after the end of antitumor treatment	1.01±0.09	0.06±0.01

Table 2. Dynamic determination of oral mucositis the severity in groups I and II.

There were higher rates of oral mucositis signs expression on 73.5 % in patients of group II ($p < 0.01$) than group I and to a more rapid buildup of the clinical picture of mucositis, the first clinical manifestations of which begin with the first session of irradiation ($p < 0.01$).

The obtained results during the saliva crystallography laboratory phase are presented in (table 3), and at the figures 1,2,3.

Group	Saliva crystal structure	Saliva crystallization tendency	Any structure lack
Before chemoradiotherapy therapy			
I	-	-	+
II	-	-	+
On the oral mucositis manifestations background			
I	-	-	+
II	-	-	+
After chemoradiotherapy therapy			
I	-	+	-
II	-	-	+

Table 3. Saliva crystallography in groups I and II at various stages of antitumor treatment.

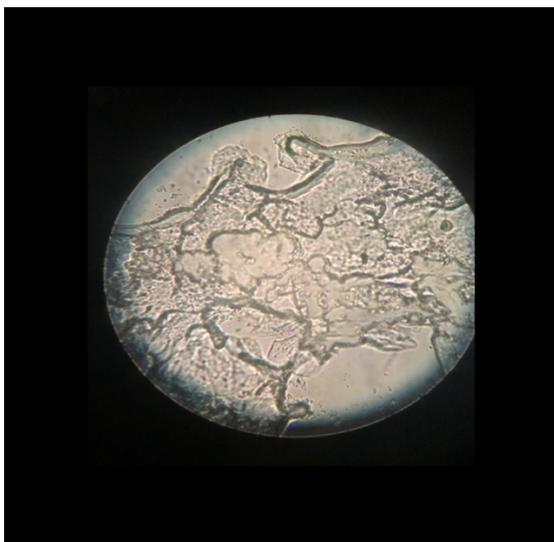


Figure 1. Patient (group I) crystallography of saliva before antitumor treatment - lack of a crystal structure of saliva.



Figure 2. Patient (group II) saliva crystallography after antitumor treatment - lack of crystal saliva structure.



Figure 3. Patient (group I) saliva crystallography after antitumor treatment - a tendency to crystal formation.

Discussion

The saliva crystallography obtained results analysis show that after the plant-based prolonged-acting drugs usage a number of patients have a tendency to crystal formation in saliva, which is not statistically confirmed, but this phenomenon can probably be considered as local treatment effectiveness confirmation²¹. The study results confirmed that crystallographic

method is effective not only in the diagnosis of the functional state of the mucous membrane, but also in the diagnosis of oral diseases of various etiologies, including cancer.

The saliva crystallographic picture patients with oral mucosal cancer changed significantly during complex treatment, including drug, radiation and local chemotherapeutic effects using ultrasound, partial regression of the tumor occurred (a decrease in volume by more than 50%). This was expressed in the suppression of the structure formation of the main signs of the systemic level (absence of a salt center, amorphization, anomaly of the marginal zone) with the growth of a malignant tumor of the oral cavity. The oral cavity bio-liquid purification from toxins and pathogenic substances contributed to the structuring of the marginal zone and the appearance of a system of radial cracks as a criterion for increasing the self-organization of saliva during the transition to the solid phase. The saliva morphostructure study simplicity, accessibility and informativeness make possible to use the criteria obtained to assess the effectiveness of antitumor therapy.

Morphological analysis of saliva facies is a simple, non-invasive, low-cost method for assessing the condition of the oral cavity, which is a significant advantage over other methods for determining the effectiveness of local treatment of oral mucositis. It can be considered for screening the therapeutic effects of using various methods of exposure to the mucous membrane.

Conclusion

The modern dental support effectiveness with usage of moisturizing and reparative components was proved both in clinical and laboratory studies (saliva crystallography) in the presented study. At the clinical stage, patients receiving dental support based on toothpaste based on mallow, betaine, xylitol and collagen plates with arnica, mint and sodium alginate have less pronounced clinical oral mucositis signs and one's reduction acceleration after the end of antitumor treatment, in contrast to patients did not one's.

Informed consent:

All patients signed an informed consent for research and data processing upon admission

to the hospital. The study was conducted in accordance with the Declaration of Helsinki.

Declaration of Interest

The authors report no conflict of interest.

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