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IMPROVED DIAGNOSIS FOR ORAL MUCOSAL TUMORS IN THE DENTIST'S OFFICE

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ABSTRACT — Based on currently available literature, clinical examination remains the major method when handling cases of suspected malignancy. However, this method does not allow diagnosing cancer, due to which a large group of patients with possible oral mucosa cancer are referred to an oncologist. The search and use of affordable non-invasive methods for early diagnosis of oral mucosa tumors is an urgent issue facing the health system. The study involved analyzing 134 records of outpatients examined at the Samara Regional Oncological Clinic who were referred by dentists within 2014-2019 from the local polyclinic in Samara due to detection of tumors in oral mucosa and who underwent a biopsy. The patients were divided into two groups according to the examination methods. The inclusion criteria were: detection of various superficial oral mucosa neoplasms; referral from the dentist. The exclusion criteria were as follows: patients with submucosal oral cavity neoplasms referred to the oncologist by other medical specialists or self-referred patients. The control group included 63 patients who, after a conventional examination (including interview, examination, palpation), underwent an incisional biopsy followed by morphological examination at the oncologist's office. In the major group, in 71 patients at their respective initial dental appointments a special examination algorithm was applied. This algorithm entailed an assessment of the identified risk factors. Indications for biopsy were identified using the histological verification index (HVI). Apart from the conventional examination methods (interview, examination, palpation), autofluorescence stomatoscopy was used, this being done for the purpose of differential diagnostics of inflammation, precancerous and malignant issues, depending on the glow type. In the main group, the initial stages of oral mucosa cancer were detected in 17 patients after biopsy; in the control group – in 4 patients (p=0.004). The developed algorithm used for scoring the patient's clinical examination data combined with autofluorescence stomatoscopy allowed diagnosing accurately (90% of reliability) precancerous and cancerous diseases, as well as to use invasive research methods (biopsy) strictly following the indications.
Aim of study: to improve diagnosis of oral mucosa neoplasms through improvement of the examination algorithm.

KEYWORDS — oral mucosa (OM), precancer, cancer, histological verification index (HVI).

INTRODUCTION

High prevalence of dental diseases, their progressiveness, individual differences in anatomy, the variety of nosological forms — all this complicates the early diagnosis of pathology in the maxillofacial region [1-6]. The possibilities of additional examination methods allow us to differentiate the effects of etiological factors, clarify various aspects of pathogenesis, study the effect of the drugs used, conduct early diagnosis, and personalize the treatment of a particular patient [7, 8].

One of the priority areas in medicine is the use of non-invasive non-contact optical technologies. Optical research methods used in dentistry (stomatoscopy and photoscopy; capillaroscopy method; ultrasound Doppler sonography; laser fluorescence diagnostics; laser Doppler flowmetry; optical tissue oximetry), in terms of their information content, visualization are not inferior to radiation methods. Insufficient knowledge of the optical properties of pathological tissues in various organic and functional disorders requires additional medical and biological research [9, 10].

Statistics shows that over 355 new cases of oral mucosal cancer are registered annually globally [11]. In 2018, the total number of cases registered with OM cancer in Russia was 9518, while the Samara region accounted for 199 patients. OM cancer, which is ranked 18th in the overall cancer occurrence structure, the diagnosis of OM cancer was confirmed morphologically in 97% of Russians [12]. Even though OM tumors belong to external locations, the share of advanced stage cases is still quite high reaching 62% (in Russia). The major reasons behind OM cancer neglect involve lack of proper oncological awareness among dentists, general public education, screening programs [13, 14, 15]. The current literature witnesses that clinical examination still remains a major method employed in case of suspected malignancy [16, 17]. This method, however, does not allow delivering a final diagnosis, while most patients with suspected OM cancer are referred to an oncologist for a biopsy, which, in turn, may result in excessive diagnostics [18, 19]. OM neoplasms biopsy is an invasive method, which involves obtaining tissue samples for histological examination, thus trying to ensure differential diagnostics and establishing a reliable diagnosis [20, 27, 28]. The procedure in some cases leads to unfavorable events, so it should be carried out while sticking strictly to certain indications — first of

all, in case a malignant OM issue cannot be excluded. The resulting histological conclusion determines the correct diagnosis, further due and timely treatment as well as the disease outcomes forecast. The somatoscope autofluorescence method has been known for a long time as a tool for diagnosing OM tumors. There have been numerous respective research publications, nationally and internationally, yet they featured no relation to the available methods such as interview and clinical examination [21, 22, 23]. Given that, the authors developed (2017) an interview algorithm with an application (#2019133760 of 08/11/2019) submitted for an invention patent *A method to identify indications for the red lip border neoplasms and the oral mucosa histological verification in the dentist's office*.

MATERIALS AND METHODS

The study was based on the analysis of 134 records of patients who underwent examination at the Samara Regional Clinical Oncological Clinic (Samara, Russia) in the period of 2014–2019 due to referrals by dentists from the local clinics because of suspected OM neoplasms. All of them underwent respective biopsy procedures. The patients were divided into two groups depending on the examination methods used. The control group included 63 patients who were referred by dentists within 2014–2016 as diagnosed with OM neoplasms. After a conventional examination procedure, which included an interview with clarification of complaints, a visual examination and palpation, an incisional biopsy was performed followed by a morphological study at the oncological clinic. In the main group (71 patients) we applied a specially developed examination method conducted at an initial dental appointment (along with an interview and a visual examination). The newly introduced method included a point-based assessment of the detected risk factors thus determinating the indications for biopsy as well as the histological verification index (HVI). In addition to the conventional examination methods (an interview, a visual examination and palpation), autofluorescence stomatoscopy was used for the purpose of differential diagnostics of inflammatory and precancerous lesions and cancer. Incisional biopsy in both groups was performed under local anesthesia with the use of otorhinolaryngological conchotomes, followed by a morphological study. Incisional biopsy in the main group was applied only to patients with HVI exceeding 5 points. The inclusion criteria were: primary referral by a dentist with OM superficial neoplasms. The exclusion criteria included cases referred by other medical specialists, self-referred, as well as those who refused to be examined, as well as cases of oral submucosal neoplasms. The patients were comparable by sex M/F 3:1 (p=0.858); age — in the control group 63+2.8 yrs, in the main group — 71 = 2.8 yrs; localization (Pearson criterion — 2.7567; p=0.8386). The newly applied method used in the main group was presented as a protocol with anamnestic data identified, an examination performed, the palpation result evaluated, as well as an examination performed with an AFS400 autofluorescent lamp (manufacturer: *Polyronik*, Moscow).

Each method in the protocol is evaluated subject to a point-based system. To facilitate and fix the final score, the HVI was used. The index value is recorded in the column with a letter mark of the lesion topographic location. A separate protocol is prepared as per each identified focus, with a respective index calculated. In the event the index is below 5, then follow-up and treatment at the dentist are administered, followed by another examination; in case the value was 5 or above, a biopsy of OM neoplasms was recommended. The main criterion for evaluating the effectiveness of this examination algorithm was the confirmed diagnosis of precancerous issues or cancer after biopsies and morphological examination. The indicators that were evaluated included the type of the complaint presented, pathological processes noted through the examination, the rate of precancerous diseases, malignant tumors and the degree of cancer after a histological conclusion. The study employed multivariate models of logistic regression in patients with oral mucosa lesions. The significance criterion was $p<0.05$ (the p-value below 0.05 was considered statistically significant). All statistical analysis procedures were performed using Statistica 10.0.

RESULTS AND DISCUSSION

The evaluation of the complaints of the patients of the main and control groups enabled their differentiation. Patients in the main group mentioned tumors less often than those in the control group (0.54 and 1.17 times, respectively). Pain was reported in the main group (M1) in 23.9% of cases, while in the control group (M2) it was reported in 47.6% of cases. Discomfort, as a condition scored high in both groups. Symptoms like sensations of burning and itching were observed equally in both groups. Table 2 offers a comparative view at the symptoms identified through the clinical examination both in the main group (M1) and in the control group (M2). Changed oral mucosa color was 0.82 times more common in the main group (54.9% vs. 28.4%); plaque was an issue observed equally in the two groups (62.0% and 60.3%), while hyperkeratosis was observed in 45.1% and in 58.7% of cases, respectively. The control group featured significant prevalence of erosions (55.6%) if compared to

Table 1. *Distribution (%) of complaints reported at the clinical examination, the main group (M1) and the control group (M2)*

Complaint Group		Tumor	Pain	Discomfort	Burning sensation	Itching	Bleeding
M1	Identified	35.2%	23.9%	64.8%	40.8%	29.6%	7.04%
	Not identified	64.8%	76.1%	35.2%	59.2%	70.4%	92.96%
	Difference	->0.54	->3.17 times	+>1.84 times	->1.45 times	->0.98 times	->13.2 times
M2	Identified	53.9%	47.6%	80.9%	42.9%	39.7%	22.2%
	Not identified	46.1%	52.4%	19.1%	57.1%	60.3%	77.8%
	Difference	+>1.17 times	->1.1 times	+>4.25 times	->1.33 times	->1.52 times	->3.5 times

Table 2. *Comparative features (%) of the disease symptoms identified through the clinical examination, the main group (M1) and the control group (M2)*

Oral mucosa examination		Changed mucosa color	Mucosa moisture (glare)	Plaque			Pathological issues			
				Present	Removable	Non-removable	Hyper keratosis	Hyper plasia	Atrophy	Erosion / ulceration
M1	Identified	54.9%	43.7%	62.0%	31.0%	28.2%	45.1%	31.0%	12.7%	36.6%
	Not identified	45.1%	56.3%	38.0%	69.0%	71.8%	54.9%	69.0%	87.3%	63.4%
	Difference	+>0.82 times	->1.29 times	+>1.63 times	->2.23 times	->2.55 times	->1.22 times	->2.23 times	->6.9 times	->1.73 times
M2	Identified	28.4%	53.9%	60.3%	33.8%	36.5%	58.7%	17.5%	11.1%	55.6%
	Not identified	71.4%	46.1%	39.7%	66.2%	63.5%	41.3%	82.5%	88.9%	44.4%
	Difference	->2.5 times	+>1.17 times	+>1.52 times	->3.2 times	->1.7 times	+>1.42 times	->4.7 times	->8.0 times	+>1.25 times

the main group (36.6%). Hyperplasia and atrophy rate varied from 11.1% to 31.0% of cases.

Thus, complaints involving pain, burning sensation, discomfort, and erosions were more frequent in the control group, whereas in the main group, plaque and tissue hyperplasia were more often identified. Given our observations, the pathological conditions of the oral mucosa localized to a greater extent on the tongue, both in the control (46%) and in the main (47%) groups, which does not contradict the data available from the currently available studies [12, 15]. After the biopsies and the obtained histological conclusion in the control group, precancerous diseases as a diagnosis were confirmed in 18 patients in the main group as well as in 36 patients in the control group, whereas the difference was significant (p=0.016). In the main group, in turn, malignant OM issues were diagnosed in 28 cases, while in the comparison group — in 14 (p=0.051).

Inflammation was observed in 7 patients in the main group and in 31 patients — in the control group (p=0.001) (Fig. 1). In the main group, the initial stages of OM cancer were detected in 17 patients after biopsy, while in the control group — in 4 patients (p=0.004). There were no significant differences in diagnosing advanced stages in the comparison groups (11 patients in the control group and 10 — in the main one) (Fig. 2). Therefore, patients with OM inflammations appear as the greatest issue in terms of diagnosing, especially when talking of differential diagnosis, for primary care dentists, and these patients are most often referred unreasonably to undergo invasive examination. Speaking in general, this method, if employed for identifying indications for histological verification of the vermillion border and oral mucosa issues at the dentist's office, allowed confirming precancerous and malignant oral mucosa issues in 90 % of the cases within the main group, whereas in the comparison group, the traditional examination produced a similar result in 51% of cases only.

If comparing the rate of false-positive outcomes in diagnosing precancerous and malignant diseases in both groups, while using traditional examination methods vs. the new one, there were some significant

differences identified (p=0.001). From the stance of early diagnostics, or in terms of secondary prevention, to be exact, where primary-care doctors are employed mostly, the detection of precancerous and malignant tumors in the main group (using the new method) featured significant differences compared to the traditional method. A number of previous studies claim that visual examination cannot be viewed as a diagnostic test when it comes to differential diagnostics, so there are also additional fluorescent and a number of other tests used, which, given our observations, proved effective when combined with the available conventional traditional ones [22, 24, 25, 26].

CONCLUSION

Using an improved algorithm for examining patients with OM diseases combined with autofluorescence somatoscopy we have identified with a high precision (90%) precancerous and cancerous tumors. It enabled us more efficient detecting initial stages of OM tumors as compared with conventional examination methods (24% and 5%, respectively). Besides, it allowed avoiding invasive methods — biopsy — unless it was indicated.

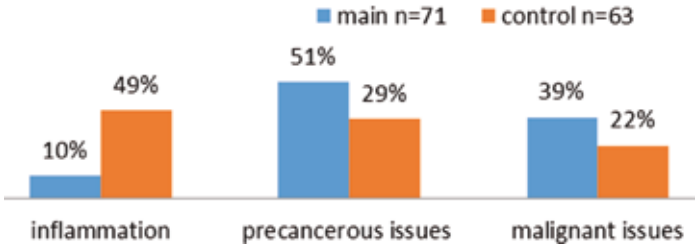

Fig. 1. Distribution within group by diagnosis

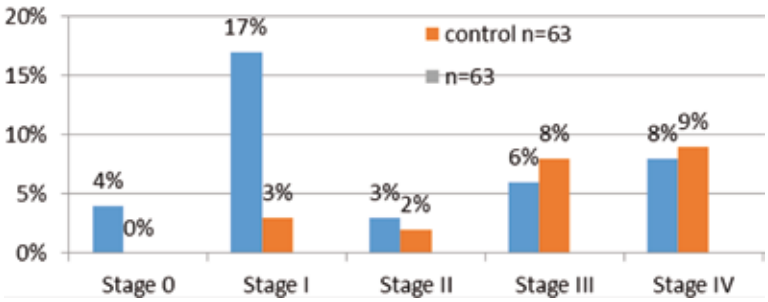

Fig. 2. Distribution within group by cancer advance

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