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ASSESSMENT OF THE EFFECT OF LOCAL TREATMENT ON THE FREQUENCY OF CELLS WITH NUCLEAR ABNORMALITIES IN THE CYTOGRAM OF BUCCAL EPITHELIUM IN PATIENTS WITH AN EROSIVE AND ULCERATIVE FORM OF LICHEN PLANUS OF THE ORAL MUCOSA (PART 1)

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Oral Lichen Planus (OLP) is a common chronic inflammatory disease with a high risk of malignization. Early diagnostic tests of erosive and ulcerative form (ECF) of the LP, timely pharmacotherapy are the key to success in the treatment of this form of dermatosis. The cytologic research method is one of the methods by means of which it is possible to obtain the results and adjust the scheme of medication symptomatic treatment in the future. **The aim of research** is to determine the effect of local treatment on the frequency of cells with nuclear abnormalities in the cytogram of buccal epithelium obtained from the reticular mesh area and from the surface of erosions in patients with the erosive and ulcerative form of the Lichen Planus in the oral cavity mucosa lining. **Materials and methods.** In the cytogram of buccal epithelium, cytogenetic indicators (micronucleus, tongue-type protrusion, and broken egg-type protrusion), indicators of nucleus destruction (karyopyknosis, karyorrhexis, karyolysis), and indicators of nuclear proliferation (notching) were assessed. **Results.** The developed method of local treatment of the erosive and ulcerative form of the Lichen Planus contributed to a more significant decrease in the frequency of cells with nuclear proliferation in the form of notches, compared to the group of patients treated according to clinical recommendations ($p=0.05$), and significantly decreased the frequency of cells with micronuclei ($p<0.01$), the frequency of degenerative change of the nucleus at $p<0.05$. Both methods of local treatment were effective, however, in clinical subgroups of patients with high titers of Candida spp. detected in the oral microbiota, the effect of local treatment in the form of ozone therapy, contributed to a decrease in the frequency of the cytogenetic indicator in the form of micronucleus protrusion (at $p<0.1$), nucleus notching (at $p<0.01$), the indicator of completion of nuclear destruction ($p<0.1$). Cytologic examination of the buccal epithelium is a non-invasive method that provides clear information about the status of the epithelial cells, in particular their DNA damage, the proliferative potential of basal cells and cell death, which are considered basic principles of cancer alertness.

Keywords: erosive and ulcerative form of Lichen Planus, buccal cytogram, ozone therapy, hyaluronic acid, corticosteroids, hyaluronic acid gel, Ora-Aid self-adhesive patch.

Introduction. The Lichen Planus (LP) involving the oral cavity mucosa lining (OCML) is a T-cell-mediated chronic inflammatory disease, with characteristic periods of relapses and remissions, and occurs as one of six variants. The reticular and erosive types of the LP are the most common in the OCML [14]. The etiological factors of the disease have not yet been discovered, although it is known that it is based on an autoimmune mechanism [20, 22].

Causes may include bad habits, somatic pathology [19, 24], menopause, depression and stress [10, 22]. The lesions are most often prevalent in females, the location on the OCML is symmetrical, and the buccal mucosa is involved in 28.1% of cases [18].

When diagnosing pathologic processes on the oral cavity mucosa lining in the form of white and/or erosive and ulcerative elements, it is necessary to screen for cancer alertness. Due to the similarity of clinical manifestations, it is sometimes difficult to distinguish benign white lesions from their pre-malignant or malignant analogues [1, 17], and the risk

of malignant transformation of the erosive and ulcerative form of the LP in the OCML according to the data represented by Iocca O. et al. (2020) is extremely low, that is 1.4% - 10% [15], the treatment and preventive measures of this form are not always effective [11].

Modern approaches to the diagnosis of pathology of the oral cavity mucosa lining include the use of various methods aimed at early screening of inflammation, as well as malignization [7]. The Buccal Micronucleus Cytome Assay (BMN Assay) provides a platform to identify individuals at high risk of malignancy by assessing markers of nuclear damage at the earliest microinvasive stage possible [23]. Histopathological examination of the involved tissue is a prerequisite for any type of OCML changes. In the research, chromosomal aberrations in the form of micronucleated cells were detected in patients with the presence of Lichen Planus clinical findings with localization on the OCML [12].

Thus, cytologic examination in cancer diagnosis of OCML pathology becomes important for choosing a rational treatment regimen. This paper considers the diagnostic criteria of the erosive and ulcerative form (EUF) of the LP in the OCML based on cytologic examination of buccal epithelium.

The goal of research is to assess the frequency of cells with nuclear abnormalities in the buccal cytogram obtained from the reticular mesh surface, hyperemia area and erosive and ulcerative elements in patients with the erosive and ulcerative form of the Lichen Planus in the oral cavity mucosa lining before and after local treatment.

Materials and methods of research. This two-center, prospective observational non-controlled study was conducted with the effective collaboration of two dermatovenerology centers of Ufa and Omsk. Patients were selected on the basis of discrete clinical features: the presence of prominent linear or reticular papules, erosive and ulcerative elements, and the presence of high titers of Candida yeast-like fungi in the oral microbiota. The record of complex dental examination included an assessment of the clinical state of the oral cavity mucosa lining, the presence of typical papules and/or erosive and ulcerative elements on the cheek mucosa, which made it possible to make a diagnosis according to ICD-10 as the erosive and ulcerative form (EUF) (L43.82) and typical (L43.80) form of the LP in the OCML. Consent for the histologic study was obtained from each patient and his/her attendants. The study was approved by the Ethics Committee of the Federal State Budgetary Educational Institution of Higher Education Bashkir State Medical University (FSBEI HE BSMU) of the Ministry of Health of the Russian Federation (Order No. 11 dated December 17, 2019).

All patients with the EUF of the LP (L43.82) in the OCML (n=86) were divided into two main clinical groups. In the composition of microbiota of erosive and ulcerative elements in patients of I (n=46) and II (n=40) main clinical groups there is a difference in the quantitative content of *Candida spp*.: in 26.08% of cases the amount from 3.0 to 5.0 Lg CFU/u, and in 47.5% of cases from 4.0-6.0 Lg CFU/u respectively.

The main clinical groups were divided into equal clinical subgroups Ia (n=23), IIa (n=23), Ib (n=20), IIb (n=20). The developed, implemented and patented complex of local treatment was used [6] (described below) for the main Ia and IIa clinical subgroups, and in the main Ib and IIb clinical subgroups the method of treatment according to the federal clinical recommendations [3] was used as a comparison. The comparison group included 25 patients with the typical form of the LP (L43.80) in the OCML and was a relative criterion of norm in the whole period of dynamic observation.

Local treatment of the EUF (L43.82) of the LP in the OCML included the use of ozone therapy on the Prozone device, applications of 0.2% hyaluronic acid gel (Hy + Al Gel), 0.5% Prednisolone ointment and Ora-Aid self-dissolving patch, which together have antiseptic, anti-candida, and anti-inflammatory properties increasing the rate of epithelialization and promoting mucosal regeneration. Erosive and ulcerative elements on the mucosa lining were treated using a preparation containing a broad-spectrum antiseptic, that is cetalkonium chloride (1 application, duration: 60 sec., 7 days), ozone therapy with the Prozone device (7 procedures, exposure duration: 6 sec., mucosa distance: 1-2 mm), as well as treatment of their surface with 0.5% Prednisolone ointment (3 times a day, 7 days). At home, the patients independently dried the mucosal surface and closed it with Ora-Aid self-adhesive patch 3 times a day until its complete dissolution, having anti-inflammatory and analgesic properties due to the active substance, that is cetalkonium chloride accelerating epithelization and mucosal regeneration due to vitamin E, 3 times a day for 6 days.

The efficacy of the local treatment complex in patients with the EUF of the LP in the OCML was assessed based on the leveling of subjective perceptions (burning, tingling and tension), changes in the composition of microbiota of the surface of erosive and ulcerative elements and pH of oral fluid. In the comparison group with a typical form of the LP in the OCML, dynamic observation was carried out, including correction of oral cavity hygiene and sanation, and elimination of traumatic factors.

Before and after local treatment (on average on day 21), we conducted a comparative cytologic study of the composition of buccal epithelium obtained by scraping with a wooden spatula from the cheek mucosa in the area of Wickham's reticular mesh (Wickham's striae) and/or the area of erosive and ulcerative elements. The level of cytoplasmic and karyological abnormalities was assessed in buccal epithelial cells. Then the following cells in the buccal cytogram were calculated: those with micronuclei, protrusions, binuclear cells (including those with twin nuclei), with chromatin condensation, karyorrhexis, karyopyknosis, karyolysis, and apoptotic corpuscles. Material for buccal epithelium examination was sampled on the first day of the study and at the end of local treatment on day 21.

Romanowsky-Giemsa staining was used for coloring. Isolated cells were selected and photographed. From 100 to 1000 isolated cells with continuous edges were analyzed. The preparations were examined at x630 magnification with immersion on a Leica DM 2500 microscope (Germany) (Fig. 1-4).

Based on the sample size, the nonparametric Mann-Whitney U test was used to match the differences between the hyperemia area and the area of erosive and ulcerative elements, which was a justifiable criterion in the context of small group size (<160 observations). For intragroup comparisons before and after local treatment, the nonparametric Wilcoxon test applied for comparison of dependent samples was used. It was considered that there were statistically significant differences in the data of the indicators of cytograms studied of buccal epithelium if the p-level of rejection of the null hypothesis was less than 0.05. The statistics and their corresponding significance levels were calculated using the 'stats' library of the R open source statistical computing environment (version 4.3.1).

Research results and discussion. The statistical analysis of nuclear aberrations in the form of cytogenetic abnormalities, indicators of destruction completion, and nuclear proliferation in the cytogram of buccal epithelium obtained from the

Table 1

Dynamics of the frequency of cells with nuclear abnormalities in the cytogram of buccal epithelium (from the reticular mesh and hyperemia area) in patients of I and II main clinical subgroups before and after the complex of local treatment

Indicators	Ia main clinical subgroup of the EUF of the LP in the OCML (suggested treatment) (n=23)	Ib main clinical subgroup of the EUF of the LP in the OCML (treatment according to federal clinical recommendations)) (n=23)	IIa main clinical subgroup of the EUF of the LP in the OCML (suggested treatment) (n=20)	IIb main clinical subgroup of the EUF of the LP in the OCML (treatment according to federal clinical recommendations)) (n=20)	Comparison group. typical form of the LP in the OCML (n=25)
1	2	3	4	5	6
Comparisons: Comparisons between groups Ia. Ib. IIa. IIb and a comparison group before treatment according to the Mann-Whitney U test *(p)*. intergroup comparisons between group Ia and Ib. IIa and IIb before treatment according to the Mann-Whitney U test (p_1). intergroup comparisons between group Ia. Ib. IIa and IIb after treatment and a comparison group according to the Mann-Whitney U test (p_2). intra-group comparisons according to the Wilcoxon test for Ia. Ib. IIa and IIb subgroups before treatment and after treatment (p_3). intergroup comparisons between group Ia and Ib. IIa and IIb after treatment according to the Mann-Whitney U test (p_4).					
Cytogenetic abnormalities					
Micronucleus before treatment	2.16±0.37 p=0.225	2.12±0.23 p=0.289	2.18±0.37 p=0.218	2.27±0.25 p=0.204	1.82±0.47
	Z=0.245, p_1=0.806		Z=0.256, p_1=0.798		
Micronucleus after treatment	1.91±0.09 p_2=0.565, p_3=0.183	2.17±0.23 p_2=0.276, p_3=0.456	1.85±0.15 p_2=0.865, p_3=0.423	2.19±0.16 p_2=0.233, p_3=0.827	
	Z=0.938, p_4=0.348		Z=1.138, p_4=0.255		
Micronucleus protrusion before treatment	1.10±0.05 p=0.149	0.92±0.34 p=0.274	1.19±0.45 p=0.254	1.17±0.36 p=0.247	0.75±0.35
	Z=0.650, p_1=0.516		Z=0.150, p_1=0.881		
Micronucleus protrusion after treatment	0.81±0.19 p_2=0.615, p_3=0.189	0.93±0.07 p_2=0.487, p_3=0.934	0.79±0.23. p_2=0.891, p_3=0.401	0.93±0.05. p_2=0.435, p_3=0.455	
	Z=0.357, p_4=0.721		Z=0.877, p_4=0.384		
(Tongue-type) Micronucleus protrusion before treatment	0.43±0.17 p=0.163	0.37±0.15 p=0.101	0.43±0.17 p=0.163	0.85±0.11 p=0.201	0.69±0.11
	Z=0.215, p_1=0.829		Z=1.178, p_1=0.239		
(Tongue-type) Micronucleus protrusion after treatment	0.66±0.24 p_2=0.799, p_3=0.207	0.71±0.29 p_2=0.786, p_3=0.160	0.68±0.40 p_2=0.898, p_3=0.417	0.71±0.23 p_2=0.842, p_3=0.472	
	Z=0.182, p_4=0.856		Z=0.384, p_4=0.701		
Indicators of nucleus destruction completion					
Karyopyknosis before treatment	6.03±0.47 p=0.812	5.87±0.41 p=0.741	6.43±0.40 p=0.399	6.40±0.33 p=0.316	6.03±0.17
	Z=0.420, p_1=0.674		Z=0.209, p_1=0.834		
Karyopyknosis after treatment	6.02±0.06 p_2=0.982, p_3=0.941	6.32±0.28 p_2=0.453, p_3=0.234	5.99±0.03$^{\&}$ p_2=0.822, p_3=0.254	6.18±0.06 p_2=0.259, p_3=0.804	
	Z=0.420, p_4=0.674		Z=1.972, p_4=0.049		
Karyorrhexis before treatment	2.95±0.34 p=0.806	2.94±0.27 p=0.814	3.85±0.14‡ p=0.009	3.67±0.21 p=0.066	2.93±0.26
	Z=0.193, p_1=0.847		Z=0.706, p_1=0.480		
Karyorrhexis after treatment	2.39±0.31 p_2=0.209, p_3=0.199	2.69±0.31 p_2=0.498, p_3=0.494	2.89±0.06*** p_2=0.877, p_3<0.001	2.85±0.05*** p_2=0.846, p_3<0.001	
	Z=0.654, p_4=0.513		Z=0.551, p_4=0.582		
Karyolysis before treatment	0.52±0.30 p=0.910	0.57±0.31 p=0.912	0.85±0.10 p=0.096	0.82±0.20 p=0.108	0.55±0.14
	Z=0.111, p_1=0.912		Z=0.091, p_1=0.927		
Karyolysis after treatment	0.56±0.12 p_2=0.977, p_3=0.895	0.67±0.15 p_2=0.569, p_3=0.589	0.56±0.13* p_2=0.932, p_3=0.048	0.72±0.15 p_2=0.132, p_3=0.299	
	Z=1.202, p_4=0.229		Z=1.389, p_4=0.165		

Окончание табл. 1

Indicators of nuclear proliferation					
1	2	3	4	5	6
Nucleus notching before treatment	4.67±0.55 p=0.802	4.41±0.42 p=0.765	4.67±0.15 p=0.741	4.96±0.05 p=0.126	4.51±0.49
	Z=1.655, p_1=0.098		Z=1.603, p_1=0.109		
Nucleus notching after treatment	4.55±0.13 p_2=0.888, p_3=0.731	4.64±0.26 p_2=0.707, p_3=0.567	4.49±0.02$^{\&}$ p_2=0.913, p_3=0.109	4.71±0.09 p_2=0.798, p_3=0.099	
	Z=0.330, p_4=0.741		Z=1.958, p_4=0.05		
Apoptotic Index (AI)					
Amount of abnormalities of the AI before treatment	17.86±2.25 p=0.811	17.21±2.13 p=0.901	19.57±1.78 p=0.420	20.14±1.51 p=0.199	17.28±1.73
	Z=0.405, p_1=0.685		Z=0.331, p_1=0.741		
Amount of abnormalities of the AI after treatment	16.90±1.14 p_2=0.309, p_3=0.405	18.13±1.59 p_2=0.367, p_3=0.355	17.25±0.66 p_2=0.908, p_3=0.211	18.29±0.79 p_2=0.261, p_3=0.349	
	Z=1.116, p_4=0.264		Z=1,715. p_4=0.086		

Note: ‡ - differences before treatment are statistically significant as compared to the comparison group indicators at p<0.01; *, **, *** - differences after treatment are statistically significant as compared to pre-treatment indicators at significance level p<0.1, p<0.05, p<0.01 and p<0.001 respectively; $^{\&}$, $^{\&\&}$, $^{\&\&\&}$ - differences are statistically significant after treatment between the main Ia and Ib, IIa and IIb clinical subgroups at p<0.1, p<0.05 and p<0.001 respectively.

surface of the reticular mesh and the hyperemia area showed that significant differences before the local treatment complex between typical and erosive and ulcerative forms of the Lichen Planus in the oral cavity mucosa lining were observed only in the indicator of completion of nuclear destruction, manifested in the disintegration of the cell nucleus into parts, and these manifestations are more evident in the II main clinical group with the predominance of *Candida spp.* in the oral microbiota (Table 1).

Local treatment provided using the developed method or according to clinical recommendations did not reveal statistical differences (*p>0.1*) in the frequency of cells with nuclear abnormalities in the cytogram of buccal epithelium in patients with erosive and ulcerative and typical forms of the LP in the OCML.

As a result of the local treatment, the cytograms of buccal epithelium showed a dynamic decrease in the frequency of cells with disintegration of part of the nucleus obtained from patients of the II main clinical group *(p<0.001)*. For patients with predominance of high titers of *Candida spp.* in the oral microbiota, the developed complex of the local treatment contributed to a significant decrease in the occurrence of cells with a degenerative change of the nucleus *(p<0.05)* in the cytogram of buccal epithelium obtained from the area of the reticular mesh and the hyperemia area. The developed method of local treatment in this category of patients also contributed to a more significant decrease in the frequency of cells with nuclear proliferation in the form of notches in the cytogram of buccal epithelium as compared to the group of patients treated according to clinical recommendations *(p=0.05)* (Table 1).

In general, according to the results of calculation of the amount of apoptotic index aberrations in the cytogram of buccal epithelium obtained from the surface of the reticular mesh and the hyperemia area, its value after treatment with the developed method was significantly lower at the level *p<0.1* as compared to the treatment according to the federal clinical recommendations. The dynamics of stabilization of the amount of the apoptotic index aberrations in the cytogram of buccal epithelium is more evident in patients with the prevalence of high titers of *Candida spp.* in the oral microbiota (Table 1).

The analysis of cytograms of buccal epithelium before and after local treatment showed that the treatment contributed to significant differences in the index of nucleus destruction, manifested in the disintegration of the cell nucleus into parts for the first and second main clinical subgroups regardless of the method applied, but for the patients of the II main clinical group with predominance of high titers of Candida spp. in the oral microbiota the effect was more pronounced (p<0.001). The effect of the developed method of local treatment was a criterion for the decrease in the frequency of nucleus destruction in the cytogram of buccal epithelium, manifested in the disintegration of the cell nucleus into parts as compared to the treatment according to clinical recommendations: for patients of the I main clinical subgroup at p<0.05, for patients of the II main clinical group at p<0.001.

The greatest effect of the developed method of local treatment was observed in patients of the IIa main clinical subgroup with predominance of high titers of Candida spp. in the oral microbiota. In the cytogram of buccal epithelium obtained after local treatment, the frequency of cells with micronuclei significantly decreased (p<0.01), and the frequency of degenerative change of the nucleus decreased at p<0.05.

In Ia and IIa clinical subgroups of patients with Candida spp. detected in the oral microbiota, in the cytogram of buccal epithelium there was observed a decrease in the frequency of a cytogenetic indicator in the form of micronucleus protrusion (at p<0.1), nucleus notching (at p<0.01), and these indicators when applying the developed method of local treatment are more significant (at p<0.1 and at p<0.001 respectively) as compared to the treatment according to clinical recommendations.

The decrease in the frequency of occurrence of the index of nuclear destruction completion in the cytogram of buccal epithelium was achieved only in the group of patients with predominance of Candida spp. in the oral microbiota and those who obtained the developed method of local treatment (IIa subgroup) at the significance level p<0.1.

When calculating the amount of the abnormalities of the apoptotic index, its

Table 2

Dynamics of changes in the frequency of cells with nuclear abnormalities in the cytogram of buccal epithelium (from the surface of erosive and ulcerative elements) in patients of I and II clinical subgroups with the erosive and ulcerative form (L43.82) of the Lichen Planus (LP) in the oral cavity mucosa lining (OCML) before and after the treatment

Indicators	Ia main clinical subgroup of the EUF of the LP in the OCML (suggested treatment) (n=23)	Ib main clinical subgroup of the EUF of the LP in the OCML (treatment according to federal clinical recommendations) (n=23)	IIa main clinical subgroup of the EUF of the LP in the OCML (suggested treatment) (n=20)	IIb main clinical subgroup of the EUF of the LP in the OCML (treatment according to federal clinical recommendations)) (n=20)
Comparisons: Intergroup comparisons between group Ia and Ib, IIa and IIb according to the Mann-Whitney U test (p_1), intra-group comparisons according to the Wilcoxon test for subgroups Ia and Ib, IIa and IIb before treatment and after treatment (p_2), intergroup comparisons between group Ia and Ib, IIa and IIb before treatment according to the Mann-Whitney U test (p_3).				
Cytogenetic abnormalities				
Micronucleus before treatment	2.35±0.25	2.33±0.18	2.92±0.17	2.84±0.19
	Z=0.134. p_1=0.893		Z=0.206. p_1=0.837	
Micronucleus after treatment	1.84±0.09, p_2=0.204	2.05±0.13, p_2=0.223	1.99±0.14$^{**,\&}$, p_2=0.002	2.54±0.09, p_2=0.199
	Z=1.007, p_3=0.314		Z=2.095, p_3=0.036	
Micronucleus protrusion before treatment	1.18±0.32	1.24±0.28	1.27±0.26	1.19±0.25
	Z=0.201, p_1=0.841		Z=0.245, p_1=0.806	
Micronucleus protrusion after treatment	0.74±0.05, p_2=0.187	0.79±0.04, p_2=0.202	0.77±0.06, $^{\&}$, p_2=0.055	0.98±0.06, p_2=0.093
	Z=0.177, p_3=0.860		Z=1.945, p_3=0.052	
(Tongue-type) Micronucleus protrusion before treatment	0.64±0.04	0.60±0.07	0.95±0.05	0.85±0.11
	Z=0.145, p_1=0.885		Z=1.178, p_1=0.239	
(Tongue-type) Micronucleus protrusion after treatment	0.68±0.02, p_2=0.877	0.68±0.03, p_2=0.819	0.70±0.04**, p_2=0.004	0.68±0.05, p_2=0.220
	Z=0.024, p_3=0.981		Z=0.181, p_3=0.856	
Indicators of nucleus destruction completion				
Karyopyknosis before treatment	6.51±0.39	6.67±0.40	6.90±0.33	6.89±0.28
	Z=0.311, p_1=0.756		Z=0.108, p_1=0.914	
Karyopyknosis after treatment	6.14±0.06, p_2=0.314	6.29±0.05, p_2=0.345	6.18±0.06, $^{\&}$, p_2=0.078	6.44±0.07, p_2=0.312
	Z=1.412, p_3=0.158		Z=1.962, p_3=0.049	
Karyorrhexis before treatment	4.06±0.28	4.18±0.21	5.67±0.21	5.79±0.18
	Z=0.821, p_1=0.412		Z=0.760, p_1=0.447	
Karyorrhexis after treatment	3.14±0.08$^{**,\&\&}$, p_2=0.009	3.59±0.08*, p_2=0.05	3.35±0.09$^{***,\&\&\&}$, p_2<0.001	4.39±0.16***, p_2<0.001
	Z=2.212, p_3=0.027		Z=3.451, p_3<0.001	
Karyolysis before treatment	0.72±0.15	0.71±0.10	1.08±0.13	1.04±0.14
	Z=0.094, p_1=0.921		Z=0.181, p_1=0.856	
Karyolysis after treatment	0.64±0.06, p_2=0.377	0.66±0.07, p_2=0.404	0.72±0.08*, p_2=0.011	0.89±0.06, p_2=0.211
	Z=0.164, p_3=0.869		Z=1.093, p_3=0.274	
Indicators of nuclear proliferation				
Nucleus notching before treatment	4.62 ± 0.09	4.70±0.07	5.16±0.09	5.27±0.08
	Z=1.003, p_1=0.316		Z=1.062, p_1=0.288	
Nucleus notching after treatment	4.55±0.07, p_2=0.234	4.59±0.07, p_2=0.310	4.65±0.07$^{***,\&\&\&}$, p_2<0.001	5.03±0.04*, p_2=0.045
	Z=0.217, p_3=0.828		Z=3.319, p_3<0.001	
Apoptotic Index (AI)				
Amount of abnormalities of the AI before treatment	20.08±1.52	20.43±1.31	23.95±1.24	23.87±1.23
	Z=0.211, p_1=0.833		Z=0.205, p_1=0.838	
Amount of abnormalities of the AI after treatment	17.73±0.43$^{\&}$, p_2=0.234	18.65±0.47, p_2=0.453	18.36±0.54$^{***,\&}$, p_2<0.001	20.95±0.53, p_2=0.069
	Z=1.678, p_3=0.093		Z=2.478, p_3=0.013	

significant decrease after local treatment (at $p<0.1$) was observed for the group of patients with candidiasis regardless of the method of treatment, but this effect was more pronounced with the developed complex (at $p<0.001$), and its differences in significance after treatment in IIa and IIb subgroups reaching $p<0.05$.

Thus, in patients with the EUF of the LP in the OCML the influence of the developed method of treatment contributed to the decrease in the frequency of micronucleus abnormalities in the cytogram of buccal epithelium, as well as in the indicators of nucleus destruction completion.

Discussion. During the examination of 139 male and female patients living in Ufa and Omsk, clinical manifestations of various forms of the Lichen Planus (typical, erosive and ulcerative, hyperkeratotic, bullous and atypical) were revealed on the oral cavity mucosa lining, the age of the patients varied from 31 to 60 years, 111 patients with the erosive and ulcerative (L43. 82) form of the LP in the OCML (n=86) and typical form (L43.80) (n=25) were further clinically examined by selection, which contradicts the data obtained by Irani S. et al. [16].

There are several studies investigating the frequency of micronuclei in patients with the EUF (L43.82) of the LP in the OCML, but they only assess micronuclei. Analysis of cytogram data of buccal epithelium obtained from the area of the reticular mesh and erosive and ulcerative elements before treatment showed a statistically significant increase of cells with micronuclei by 1.42 times from the surface area of erosions and ulcers in the EUF (L43.82) of the LP than from the reticular mesh area in typical form of the LP (L43.80) in the OCML ($p<0.05$). Our data are close to those obtained by Sanchez-Siles M. et al. [21].

According to the data of Serikova O. V. et al., in cytological preparations the total number of cells with abnormalities, as well as the frequency of occurrence of some nuclear aberrations (micronuclei, karyorrhexis, karyopyknosis) is higher in the EUF (L43.82) of the LP in the OCML, and the frequencies of occurrence of some indicators of nucleus destruction (karyolysis and perinuclear vacuoles) were lower than in the control group ($p<0.05$). On the surface of the erosive and ulcerative elements, the number of cells with abnormalities prevailed as compared to the area without abnormalities ($p<0.01$) [1, 2, 4]. In a study of patients with a clinical diagnosis of the EUF of the LP in the OCML, Buajeeb et al. (2007) also found a significantly increased frequency of micronuclei [9]. During clinical and laboratory research we took into account the data of cytograms of buccal epithelium obtained in 86 patients with the EUF (L43.82) of the LP in the OCML. When analyzing the data of cytograms of the reticular mesh surface and hyperemia area before and after local treatment significant differences in the index of nuclear destruction completion were obtained, manifested in the disintegration of cell nucleus into parts, and the studied index was more obvious in patients of the II main clinical group with predominance of Candida spp. in the oral microbiota. The effect of the developed method of local treatment [6] was an important criterion contributing to the decrease in the frequency of nucleus destruction in the cytogram of buccal epithelium for patients of the I main clinical group at $p<0.05$, and for patients of the II main clinical group at $p<0.001$. In the cytogram of buccal epithelium the frequency of cells with karyological aberrations, that is micronuclei ($p<0.01$), degenerative change of the nucleus at $p<0.05$ significantly decreased. In cytograms obtained from the surface of erosive and ulcerative elements of patients of Ia and IIa clinical subgroups with Candida spp. detected in the oral microbiota, there was observed a decrease in the frequency of the cytogenetic index in the form of micronucleus protrusion (at $p<0.1$), nucleus notching (at $p<0.01$), and these indicators when applying the developed method of local treatment were more significant (at $p<0,1$ and at $p<0.001$ respectively), the decrease in the frequency of the index of nuclear destruction completion was achieved only in IIa clinical subgroup at significance level $p<0.1$.

Manifestation of chronic inflammation on the oral cavity mucosa lining in the EUF (L43.82) of the LP mainly has signs of a macrophage response and is subjected to oxidative stress, which contributes to the production of endogenous reactive oxygen and nitrogen species, and their imbalance has a direct toxic effect on tissues. This induces a proliferative response, which in turn promotes genetic damage, increasing the degree of error probability in DNA replication by increasing genetic instability in it [13], which is consistent with our data.

Assessment and analysis of cytogenetic abnormalities, proliferation and apoptosis in the cytogram of buccal epithelium can be used as a differentiated approach in the diagnosis, and control of the course of various forms of the Lichen Planus in the oral cavity mucosa lining and adherence to the principles of cancer alertness [5].

Karyopyknosis, karyorrhexis and karyolysis is the terminal stage of epitheliocyte destruction. The decrease in the number of these cells in the main clinical groups with the developed method of local treatment correlates with the decrease in the degree of hyperkeratosis and restoration of the structure of the oral mucosa.

Conclusion. The effect of the developed method of local treatment, including a complex of ozone therapy on the Prozone device, applications of 0.2% hyaluronic acid gel (Hy + Al Gel), 0.5% Prednisolone ointment and closure of the surface of erosive and ulcerative elements with Ora-Aid self-dissolving patch contributes to the decrease in the frequency of cells with proliferation of the nucleus in the form of notches, decreased frequency of cells with micronuclei ($p<0.01$), degenerative changes of the nucleus ($p<0.05$) as compared to the group of patients treated according to clinical recommendations ($p=0.05$). In clinical subgroups of patients with prevalence of high titers of Candida spp. in the composition of the oral microbiota, the influence of the developed method contributed to the decrease in the frequency of micronucleus protrusion (at $p<0.1$), nucleus notching (at $p<0.01$), and the index of nuclear destruction completion ($p<0.1$).

In conclusion, cytologic examination of buccal epithelium is a sensitive, non-invasive method that provides clear information on the status of epithelial cells, in particular their DNA damage, the proliferative potential of basal cells and cell death, which are considered basic principles of cancer alertness.

Thus, cytogenetic monitoring of patients with dermatosis is of special importance as it allows to control the dynamics of the frequency of occurrence in the cytogram of buccal epithelium of the indicator of nucleus destruction, that is karyopyknosis and karyorrhexis, and allows of their clinical observation in the process of local treatment and screening of the EUF (L43.82) of the LP in the OCML.

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HEALTHY LIFESTYLE. PREVENTION

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CHICKENPOX AND HERPES ZOSTER: DYNAMICS OF INCIDENCE AND APPROACHES TO PREVENTION

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The dynamics of the incidence of chickenpox and herpes zoster in the population of the Irkutsk region and the city of Irkutsk against the background of ongoing selective vaccination was studied. A descriptive epidemiological study was conducted according to state statistical reporting based on materials from the Irkutsk region and the city of Irkutsk for 2013-2022. The calculation of predictive values was made using regression equations, the statistical significance of differences in intensive indicators was assessed by 95% CI. Against the background of a decrease in the incidence of chickenpox, in 2021-2022. There was an increase in the indicator among different age groups of the population, the most significant among children under 6 years of age. According to the forecast, in 2023 the incidence rate will not change significantly. Selective vaccination tactics do not significantly affect the incidence of chickenpox (p = -0.217; -0.7; p>0.05). The incidence of shingles in the region exceeds the national level. Taking into account the continuing epidemiological trouble for chicken pox in the region and the data of forecast calculations, it is necessary to adjust the existing vaccination programs, including gradually expanding the contingents to be vaccinated.

Keywords: chicken pox, shingles, incidence, vaccination.

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Introduction. Chickenpox and herpes zoster (HZ) are two independent and at the same time different in clinical manifestations nosological forms, the etiolog-