

Experience of the Use of Photodynamic Therapy in the Treatment of Chronic Traumatic Lesions of Oral Mucosa

Doświadczenie w zastosowaniu terapii fotodynamicznej w leczeniu przewlekłych pourazowych zmian błony śluzowej jamy ustnej

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SUMMARY

Aim: To evaluate the therapeutic effectiveness of the use of photodynamic therapy in chronic traumatic lesions of oral mucosa.

Materials and methods: Clinical examination and treatment of 67 patients aged 18-65 years with erosive-ulcerative lesions of oral mucosa were carried out. Treatment of patients in the main group was performed using photodynamic therapy. Treatment of patients of the control group was carried out according to the standard method. The results of treatment were evaluated by clinical and cytological parameters.

Results: In all patients of the main group with chronic traumatic erythema, already on the second day of treatment, complaints of pain when talking and eating completely disappeared, and on the third day in 100% of patients the affected mucosa had no pathological changes. In patients with erosive-ulcerative lesions, complete clinical recovery in the main group was observed on the 3-4th day of treatment, in the control group – on the 7-10th day. The results of cytological examination, namely the absence of young epithelial cells of stages 1 and 2 of differentiation, a significant decrease of intermediate maturity cells (stages 3 and 4) and a similar increase of mature cells (stages 5 and 6), indicated the acceleration of mucosal regeneration in patients of the main group compared to the control group.

Conclusions: The use of photodynamic therapy in the treatment of traumatic oral mucosa lesions contributed to the acceleration of elimination of clinical manifestations of chronic mechanical injuries and the normalization of parameters of cytological characteristics of epithelial cells in patients of the main group compared to the group of standard treatment.

Key words: photodynamic therapy, traumatic lesions, oral mucosa, cytological research

Słowa kluczowe: terapia fotodynamiczna, zmiany pourazowe, błona śluzowa jamy ustnej, badania cytologiczne

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INTRODUCTION

Despite certain achievements in the treatment and prevention of chronic traumatic lesions of the oral mucosa, the search for more advanced and effective methods of treatment continues. One of the perspective directions for solving this problem is photodynamic therapy (PDT), which is based on the use of low-intensity laser radiation and substances – photosensitizers [1, 2]. Numerous scientific studies indicate the complex action of laser light, that under certain conditions causes many biochemical processes in the body: it blocks the inflammatory process, helps to clean erosive foci from the products of tissue decay, reduces the content of inflammatory mediators in the affected areas, improves metabolic and reparative processes [3-6]. Because the mechanism of PDT action is due to free-radical reactions occurring in the tissues with accumulated photosensitizer,

the process has a local character, limited by radiation zone and has no systemic effect. Another advantage of PDT is the ability to reduce the pathogenicity of the microflora and increase its sensitivity to the action of antibacterial drugs, as well as the absence of the development of microbial resistance and microbiocenosis disorders [7, 8]. Taking into account the availability of pathological focus on the oral mucosa for laser radiation, it is advisable to use it for PDT in the treatment of erosive-ulcerative lesions. An important role in improving treatment of oral mucosa diseases is played by the use of methods of adequate control over the effectiveness of treatment measures. In this direction, it is promising to use a cytological method that provides objective information about the morphofunctional state of oral mucosa in its lesions of various types and in the dynamics of treatment [9].

AIM

To evaluate the therapeutic effectiveness of the use of photodynamic therapy in chronic traumatic lesions of oral mucosa.

MATERIALS AND METHODS

Clinical examination and treatment of 67 patients aged 18-65 years with traumatic lesions of the oral mucosa were carried out. Among them, in 35 patients the chronic traumatic erythema was diagnosed, in 19 patients – traumatic erosion, and in 13 patients – decubitus ulcer. The patients were divided into two groups: the main group (n=32) and the control one (n=35). In both groups treatment was stated with the elimination of traumatic factors. The patients of the main group underwent with non-contact laser radiation of the affected areas with the Picasso diode laser “AMD Lasers” (USA) with a wavelength of 940 ± 15 nm in a constant mode with a power range of 0.5 W/cm^2 when using non-activated fiber “Program 4” [10]. Exposure was 2 minutes on each zone, number – 5 procedures daily. As a photosensitizer, a 0.1% aqueous solution of methylene blue was used, which exhibits antiviral, antibacterial, and antifungal effects and has a minimal damaging action on the cells of oral mucosa. Treatment of the control group included rinsing with Paroex 0.06% solution for 1 minute 2 times per day, application of Cholisal gel and sea buckthorn oil for 20 minutes 2 times per day.

Cytological research methodology and its assessment were carried out according to the recommendation by GV Banchenko et al. [8]. Mathematical processing of cytograms was determined by the formula: $\text{IDC} = 1a + 2b + 3c + 4g + 5d + 6e$, where IDC – the cell differentiation index; 1-6 – digital values of the degree of cells differentiation, a-e – the percentage of cells corresponding to the maturation stage.

The analysis of statistical data was carried out using the method of the Student's t-test according to the principle of variation statistics. Values of $p < 0.05$ were considered statistically significant.

The research was carried out in compliance with the main provisions of the “Rules of Ethical Principles of Scientific Medical Research Performing with Human Participation”, approved by the Declaration of Helsinki, ICH GCP, EU Directive № 609, orders of the Ministry of Health of Ukraine № 690 dated 09/23/2009, № 944 dated 12/14/2009, № 616 dated 08/03/2012. The research protocol was approved by the Biomedical Ethics Committee of National Pirogov Memorial Medical University, Vinnytsya.

RESULTS

During the clinical examination, in 35 patients with chronic traumatic erythema the edema and hyperemia of the oral mucosa were revealed. Localization of lesions corresponded to the action of an irritating factor (Figure 1). Regional lymph nodes in 6 (17.1%) of cases were enlarged, mobile, not fixed with underlying tissues and painful on palpation.

Clinical manifestations of chronic traumatic erosion, which were diagnosed in 19 patients, were characterized by swelling and hyperemia of the mucosa with single erosions of an oval shape, covered with a fibrinous slough, sharply painful. Lymph nodes in 68.4% of patients were enlarged and painful on palpation.



Figure 1. Patient Z. Diagnosis: Chronic traumatic erythema of oral mucosa before treatment



Figure 2. Patient P. Diagnosis: Decubitus ulcer before treatment

A decubitus ulcer was diagnosed in 13 patients. All patients complained of pain, increased when eating and using removable dentures (Figure 2). In these patients the submandibular lymph nodes were enlarged and painful on palpation.

Positive dynamics of clinical symptoms of the disease after performed treatment was revealed in both studied groups. Thus, in 17 (100%) of patients of the main group with chronic traumatic erythema, after the elimination of the irritating factor already on the second day of treatment, complaints of pain when talking and eating completely disappeared, in 9 (52.9%) of patients there were no swelling and hyperemia on the affected surface. On the third day of treatment, in 100% of patients of the main group, the affected mucosa was pale pink in color and had no pathological changes (Figure 3). In the control group, complaints and clinical manifestations disappeared later (on the 4-5th day) after the start of treatment.

When examining all 100% of patients of the main group with erosive-ulcerative lesions, already on the second day of treatment, the absence of pain in the damage zone and disappearance of bleeding during eating were noted. On the

3rd day of treatment the redness and signs of regeneration of erosive elements on the affected mucosa were revealed in all these patients, and on the 4th day the erosions were healed, signs of inflammation were completely absent, the oral mucosa had no pathological changes (Figure 4). At that time, in the control group complaints of pain while eating and talking were present for 3-4 days from the start of treatment, recovery was observed on the 5-7th day.

For an objective assessment of mucosal injury in chronic traumatic lesions, a cytological study was carried out, based on qualitative and quantitative characteristics of development stages of epithelial cells and cytopathological changes in the cell population. From the given data (Tables 1, 2) it can be seen that after the treatment young basal and parabasal cells completely disappeared and non-nucleated cells with a high degree of keratinization prevailed, that indicated the recovery of barrier function of the oral mucosa. Thus, after treatment of the main group of patients with chronic traumatic erythema, a significant ($p < 0.001$) decrease in the specific weight of epithelial cells of intermediate transformation was revealed (from $27.17 \pm 0.57\%$ to $3.17 \pm 0.2\%$ – stage 3 and from $27.9 \pm 0.4\%$ to $10.47 \pm 0.32\%$ – stage 4) and a similar increase in cells of the late stage of differentiation (from $8.09 \pm 0.33\%$ to $53.17 \pm 0.5\%$), and as well as the cell differentiation index (from $394.25 \pm 14.2\%$ to $536.2 \pm 0.85\%$).

The main feature of cytological characteristics of impressions from the affected areas of oral mucosa with erosive-ulcerative lesions was the detection of single keratinized epithelial cells (respectively in $3.0 \pm 0.21\%$ of patients with chronic traumatic erosion and in $3.62 \pm 0.3\%$ of patients with decubitus ulcer,



Figure 3. Patient Z. Diagnosis: Chronic traumatic erythema of oral mucosa on the 3rd day of the treatment



Figure 4. Patient P. Diagnosis: Decubitus ulcer on the 7th day of the treatment

$p < 0.001$), which normally compose more than half of all cellular structures ($53.1 \pm 0.49\%$).

Along with the criteria mentioned above, a significant ($p < 0.001$) decrease in the cell differentiation index and pronounced microbial contamination of epithelial cells (Figure 5) on the background of increased total cellularity can be considered as a serious pathological process that needs active treatment.

The most significant changes in the parameters of cytological characteristics of the oral mucosa epithelium were revealed after course of therapy in patients of the main group with chronic traumatic erosion and decubitus ulcer. At the same time, all average statistical values of the percentage of squamous epithelial cells in the oral mucosa impressions, as well as the index of cell differentiation after treatment with a significance degree of 99-99.9% were differed from those before treatment. On the background of a decrease in total cellularity, signs of cell contamination by microorganisms disappeared. This indicated the high treatment efficiency of chronic mechanical injury of oral mucosa by PDT.

At the same time, assessment of the level of epithelial cell differentiation in the impressions of the oral mucosa in patients of the control group after traditional treatment did not reveal significant changes in parameters. In patients with chronic traumatic erosion of the control group, although young cells of the 1st and 2nd stages of maturity disappeared and the number of intermediate cells of type 1 decreased by half, compared to baseline ($p < 0.01$), and the cell differentiation index significantly increased (from $329.7 \pm 8.3\%$ to $504.9 \pm 1.5\%$, $p < 0.001$), but the average statistical values of type II intermediate cells and superficial cells with pyknotic nuclei and weakly basophilic cytoplasm did not change significantly (respectively, $30.7 \pm 0.8\%$ against $27.4 \pm 4.6\%$ and 11.2 ± 0.6 against $17.7 \pm 0.7\%$, $p > 0.05$). It is obvious that the normalization of oral mucosa epithelization when using the traditional approach to the treatment of chronic traumatic erosion occurs more slowly than in the main group.

Examination of patients of the control group with decubitus ulcer revealed that in the cytograms of mucosa impressions there was a “shift to the left” in the balance of epithelial cells. Their significant number (stage 2 – $2.67 \pm 0.7\%$, stage 3 – $13.14 \pm 0.6\%$, stage 4 – $17.7 \pm 1.14\%$) and microbial contamination indicated the low treatment efficiency of patients of the control group.

Table I. Results of cytological study in patients of the main group with chronic traumatic lesions of oral mucosa

Groups of examinees (number of patients)	Stages of differentiation of epithelial cells in the main group before treatment (%)						Stages of differentiation of epithelial cells in the main group after treatment (%)							
	1	2	3	4	5	6	IDC	1	2	3	4	5	6	IDC
Chronic traumatic erythema (n=17)		2.17 ± 0.33	27.17 ± 0.57	27.9 ± 0.4	34.8 ± 0.37	8.09 ± 0.33	394.25 ± 14.2		>0.05	3.17 ± 0.2	10.47 ± 0.32	33.17 ± 0.45	53.17 ± 0.5	536.2 ± 0.85
p										<0.001	<0.001	>0.05	<0.001	<0.001
Chronic traumatic erosion (n=9)	5.07 ± 0.63	33.7 ± 1.1	18.1 ± 0.63	29.7 ± 0.62	10.5 ± 0.68	2.8 ± 0.28	311.4 ± 9.5			3.5 ± 0.45	11.4 ± 0.8	33.5 ± 1.27	51.4 ± 0.95	532.8 ± 1.4
p										<0.001	<0.001	<0.001	<0.001	<0.001
Decubitus ulcer (n=6)	18.7 ± 1.38	27.1 ± 0.65	17.16 ± 0.65	25 ± 0.68	7.98 ± 0.39	3.3 ± 0.41	292.5 ± 16.9			3.8 ± 0.65	10.6 ± 1.07	32.6 ± 1.6	52.8 ± 0.5	533 ± 2.9
p										<0.001	<0.001	<0.001	<0.001	<0.001

Note: p - the significant difference in parameters in patients of the main group before and after treatment.

Table II. Results of cytological study in patients of the control group with chronic traumatic lesions of oral mucosa

Groups of examinees (number of patients)	Stages of differentiation of epithelial cells in the control group before treatment (%)						Stages of differentiation of epithelial cells in the control group after treatment (%)							
	1	2	3	4	5	6	IDC	1	2	3	4	5	6	IDC
Chronic traumatic erythema (n=18)		1.97 ± 0.31	27 ± 0.5	28.2 ± 0.38	34.5 ± 0.63	8.07 ± 0.5	536.2 ± 0.85			4.1 ± 0.3	12.6 ± 0.8	33.8 ± 0.7	50.01 ± 0.5	534.5 ± 4.05
p										<0.001	<0.001	>0.05	<0.001	>0.05
Chronic traumatic erosion (n=10)	4.93 ± 0.54	32.2 ± 1.23	18.1 ± 0.53	30.7 ± 0.8	11.2 ± 0.6	2.87 ± 0.2	329.7 ± 8.3			7.8 ± 0.5	27.4 ± 4.6	17.7 ± 0.7	47 ± 0.9	504.9 ± 1.5
p										<0.001	>0.05	>0.05	<0.001	<0.001
Decubitus ulcer (n=7)	18.13 ± 1.86	26.8 ± 1.14	18.4 ± 0.89	26.14 ± 0.68	8.2 ± 0.31	3.65 ± 0.33	289.5 ± 10.4			13.14 ± 0.6	17.7 ± 1.14	26.2 ± 1.25	43.2 ± 1.2	499.7 ± 8.85
p										<0.001	>0.05	>0.05	<0.001	<0.001

Note: p - the significant difference in parameters in patients of the main group before and after treatment.

DISCUSSION

During the study, significant changes in cytological parameters were revealed in patients with erosive-ulcerative lesions of oral mucosa. The high treatment efficiency with PDT was indicated by a decrease in the total number of type I-II cells and a reduction their contamination by microorganisms, which is correlated with literature data on the wide antibacterial spectrum of the method. At the same time, no significant changes in clinical and cytological parameters were found in the control group after the treatment.

In patients with chronic traumatic erosion, despite the disappearance of young cells of the 1st and 2nd stages of differentiation and decreasing by half of the number of intermediate cells of type I, the average statistic parameter of intermediate cells of type II and superficial cells were not significantly changed. The patients with decubitus ulcer had a “shift to the left” in the balance of epithelial cells and microbial contamination, that indicated the low efficiency of traditional treatment [5].

Thus, the positive dynamics of cytological analysis parameters and the normalization of physiological condition of oral mucosa after the treatment of patients of the main group prove the high efficiency of chronic mechanical injuries treatment by the method of PDT using methylene blue in comparison with traditional treatment.

CONCLUSIONS

1. The use of PDT for treatment of traumatic oral mucosa lesions contributed to the elimination of the main clinical manifestations of chronic mechanical injuries on the 3rd day of treatment in patients with chronic traumatic erythema and on the 5th-7th day in patients with erosive-ulcerative lesions, in contrast to the control group, in which the main clinical manifestations disappeared on 4-5 days in patients with traumatic erythema, and on 7-10 days in patients with erosive-ulcerative lesions.
2. The identified significant changes in the parameters of cytological characteristics of epithelial cells and the reduction of their contamination by microorganisms in patients with erosive-ulcerative lesions indicated the high efficiency of PDT usage in the treatment of traumatic injuries.

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Conflict of interest:

The Authors declare no conflict of interest

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