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Justification of the Effectiveness of Plasmolifting™ Procedure in Treatment of Patients with Erosive and Ulcerative Lesions of the Oral Cavity

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Abstract: Despite the current level of development of medicine and gained practical experience, the problem of the acceleration of reparative processes in the oral mucosa is still relevant. The problem of improving the ways and means influencing the healing processes in the oral cavity remains one of the most pressing issues of therapeutic dentistry. This study involves the clinical-experimental study conducted. Clinical examination and treatment of patients involved the use of standard treatment regimen of erosive and ulcerative lesions in the oral cavity compared with autohemotherapy. Experimental part included modeling of oral mucosa wound process with further investigation of the characteristics of connective tissue regeneration in dogs divided into two groups. Clinical, morphological and cytological data suggests the effectiveness of autohemotherapy in patients with erosive and ulcerative lesions of the oral mucosa in comparison with the conventional method and that is the reason to give our preference to this method of disease treatment. Applying the autohemotherapy allows us to explain the regenerative features of the oral mucosa, indicating the feasibility and justifiability of this method.

Key words: Plasmolifting, regeneration, reparation, erosion, ulcer

INTRODUCTION

Erosive and ulcerative lesions take a special place among the pathological processes localized on the oral mucosa and vermilion border. This is due to the fact that in their treatment the practitioner is often confronted with difficulties related to the presence of patients with long-term, persistent progress of these diseases with frequent relapses (Akhmerov *et al*., 2007; Firsova *et al*., 2015a, b; Martynova *et al*., 2015).

Diagnosis and treatment issues of these states are the most difficult for dentists and other doctors. This is primaraly due to close anatomical and physiological relationship of the oral cavity with different systems of the body. Furthermore, erosions and ulcers may result from oral mucosa injury and various manifestation of somatic diseases (infection, cancer, allergies, dermatoses, etc.) and oral dysbiosis (Zhuravleva *et al*., 2015).

Erosive and ulcerative lesions of the oral mucosa as a rule, do not have specific manifestations, depending on the causative agents and their clinical findings may vary in a short period of time. There can be traced a relation between the level of oral hygiene, the presence of other risk factors and the severity of lesions (Dean *et al*., 2011).

Treatment plan for such patients is coordinated with multi-disciplinary group of doctors (general practitioner, infectious disease specialist, hematologist, oncologist). Comprehensive treatment of this disease includes measures aimed at pain and inflammation reduction and acceleration of the recovery process after the maximum possible elimination of the causative factors. However, the use of medication and physical therapy in these patients is often limited due to the presence of concomitant somatic diseases. The urgency of the problem is also determined by the fact that this type of lesion has a significant prevalence and refers to the facultative precancerous lesion with a high incidence of malignization (Akhmerov *et al*., 2007; Temkin *et al*., 2015; Firsova *et al*., 2015c).

This requires a doctor's oncologic allertness and improvement of the efficiency and timeliness of treatment. Thus, treatment of erosive and ulcerous diseases of the oral mucosa is a complex task that requires close cooperation of a dentist, a patient, a physician and other medical subspecialists (Quirynen *et al*., 2000).

The priority area in medicine is the development and application of methods and drugs that combine maximum safety and high biological activity with respect to the

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body's tissues. In this context, a very important part in the treatment of erosive and ulcerative lesions may be the methods of local stimulation of oral mucosa tissue regeneration. The method of choice can be the injections of platelet autoplasma which is a highly active biological stimulator of regenerative processes due to the platelets of various growth factors contained in its alpha-granules. Furthermore, the application of autologous plasma eliminates the possibility of infection and allergic reactions. The use of platelets-containing plasma is today one of the few opportunities to modulate and enhance wound healing process and resist an infection without the use of drugs. The dvantages of this method lie in that the autologous plasma can accelerate the recovery of the bone, cartilage and epithelial tissues as the regeneration process is universal and differs only in duration of a process. Another advantage of this method is the improvement of the microcirculation and metabolism which stimulates local immunity. In addition, platelet derived growth factors are inable to induce a cancer, since they are not mutagenic (Akhmerov *et al*., 2007).

Currently, there is information occurring in the professional literature about the use of platelet autoplasma in treating the inflammatory diseases of the maxillofacial region. Its applicability in various fields of medicine and dentistry is under consideration, based on the activation of human functional reserves reduced under the influence of either adverse environmental factors or disease (Temkin *et al*., 2014). However, clinical studies based on demonstrative data are scarce and the obtained results require further study.

For the purpose of studying the effectiveness of autohemotherapy on the regeneration of the oral mucosa, clinical and experimental study was conducted in the Department of Therapeutic Dentistry of Volga Region SMU.

MATERIALS AND METHODS

Clinical part included the examination and treatment of 60 people diagnosed with erosive and ulcerative form of lichen ruber planus in age of 40-70 years. Subject to the treatment performed, all patients were divided into 2 groups.

Group 1, a control group (30 patients) who underwent conventional medical treatment and group. An experimental group (30 patients) whose treatment included the use of autoplasma.

All patients had general dental examination and monitoring of the dynamics of reparative processes with the use of a cytological method.

The patients' examination started from the survey which included the identification of complaints and taking of disease and life history. In case of complaints identified, the patients were asked to describe in detail the nature of the sensations, their location and relation to the meal. During history taking, we found out the nature of the disease progress, possible causes of the pathology and its aggravations in particular, the presence of stressful situations and psycho-emotional stresses and physical illnesses. We paid attention to the previous treatment of this disease and its effectiveness. We found out the number of relapses, their frequency and duration.

We conducted a thorough visible examination of the oral cavity by the conventional method, using a set of dental instruments which included an assessment of hard tooth tissues, periodontal tissue and oral mucosa.

We paid particular attention to dental health and if necessary, elimination of initiating factors (sharp tooth edges, broken teeth as well as dentures made of dissimilar metals).

To conduct Plasmolifting procedure, the blood was centrifuged. After heating it in the termostat the gel is obtained. Gelled autoplasma was dissected by sterile forceps and fixed to the lesion via diplenovskoy film until complete plasma and the salve film dissolution.

Oral mucosa was evaluated on the following criteria: inflammation, hyperemia, bleeding and continuity disruption (erosion or ulcer). Studying the pathological elements, we focused particularly on the size, depth and color of the lesion. The area of the oral mucosa lesion was determined with the help of teeth impression. The impression was taken with the use of a sterile rubber and a chemical pencil and further put on graph study where the lesion area was calculated.

We applied cytological method to clarify the diagnosis and identify both the beginning of the malignization and features of the inflammatory response. The object of cytological research was the scrapings on a cotton swab. The material was further fixed on the sterile glass and smeared. The dried smears were stained with hematoxylin-eosin and examined under a microscope. Studying the obtained material, we considered the number of leukocytes, histioid elements and the nucleus structure (nuclear membrane, chromatin). We also considered the amount of coccal flora. We observed the processes of degenerative degradation and hyperkeratotic effects.

We conducted a cytology, the lesion measurement and evaluation of the clinical pattern in the two groups of patients with lichen ruber planus at the initial examination and on the 5, 10, 15 and 30th day of treatment. All information was recorded in the case record of a dental patient.

Experimental part of study was carried out on 32 dogs, each of 10 kg. The experiments were conducted with the permission of the Research Ethics Review Committee of Volgograd State Medical University (protocol No. 214-2015 of 04.29.2015).

We performed experimental modeling of the pathological process of periodontal disease by creating 1×1 cm oral mucosa defect on the maxilla left and right in the region of one premolar in the oral vestibule. Surgery was performed under intravenous anesthesia with Zoletil. The defect was made with a scalpel, forceps and chisels up to the periosteum.

All animals were divided into 2 groups: Group 1, (control) the defect healed without additional treatment; Group 2, the animals had platelet autoplasma introduced. To eliminate the influence of additional factors, related to individual characteristics of the animal, on the final result of the experiment, the observational groups were formed of the same animal species

Blood was sampled from dogs by the standard method using a tourniquet, alcohol wipes, a needle, a test-tube holder adapter, plaster and specialized test-tubes "Plasmoliphting" TM". After sampling the blood, a test tube was placed into a centrifuge "EVA 20", at 3200 rpm for 5 min. Using special test tubes "Plasmolifhting™" allowed us to obtain 1.5±0.5 mL of platelet plasma; in addition, a separating gel ensures high-quality filtration of plasma and good fixation of the erythrocyte clot.

To compare the effectiveness of PRP therapy, we performed the following procedures. The dogs of Group 2 were introduced 2.0 mL platelet autoplasm in the area of wound defect left along the transitory fold by infiltration. The wound defect right was left for monitoring and comparing the time of the epithelium regeneration. The dogs and the regeneration of the epithelium in the wound defect were controlled daily for 14 days. Results of the study were recorded in written form and by photography.

Data obtained from studies were processed by variation statistical method on the IBM PC/AT Pentium-IV Windows 2000 using the application package.

Statistica 6 (Statsoft-Russia, 1999) and Microsoft Exsel Windows 2000. Statistical analysis was performed by variation statistical method with defining the average value (M), its mean error (±m) and evaluating the significance of difference in the groups using student's t-test (t). The difference between the compared indicators was considered significant at $p<0.05$, $t\geq 2$.

RESULTS

As we can see from clinical data, in some cases the first therapeutic effect can be observed in the patients' oral cavities after a week which is manifested by improved hygienic and periodontal indices, decreased gum bleeding and hyperemia and the recovered physiological color of the gum. Some patients had no complaints, against the positive dynamics of diagnostic methods indicators (OHI-S, GI, KPI, etc). All examined patients had good oral hygiene (OHI-S = 0.24±0.02). CPI was 0.4±0.05 which corresponds to the risk of periodontal tissue disease. GI was 0.27±0.03 (mild gingivitis), DEF index was 14.5±0.7.

Both groups of patients showed positive changes during treatment. When analyzing the clinical data of therapeutic measures in patients of Group 1, we should note that the patients reported a temporary improvement at the end of their treatment (on day 30). However, the mucous membrane still had papular pattern remained and no complete epithelialization was observed in erosions and ulcers.

The assessment of changes in clinical findings of patients of Group 2 found that all patients reported no discomfort in oral cavity as well as no tightness of mucosa. Two patients of Group 2 showed complete disappearance of papular pattern and the rest had a significant reduction in its length. There also was a sharp reduction in signs of hyperemia and mucous membrane swelling in the area of the lesion.

On day 15, the patients of Group 2 showed a decrease in both area and depth of the lesion, the ulcer cleansing from necrotic plaque, the disappeared hyperemia and swelling of the mucous membrane and pale grayish color of the papular pattern. We should note that 5 patients of this group had a complete epithelialization of erosions and only a gentle papular pattern on the mucous membrane against slightly congested mucosa which indicated the disease changing into a milder form.

The analysis of the obtained during treatment cytograms, conducted in order to study the reparative processes in oral mucosa, revealed that the positive changes in the status of epithelial cells in the Group 2 of patients occurred earlier than in the Group 1.

Already on the day 5, cytological findings in the Group 2 were characterized by a decrease in both signs of degenerative changes in the cells and the number of coccal flora as well as by the appearance of epithelial cells arranged in layers rather than separately or in groups. Patients of Group 1 showed no cytological changes by that time. During treatment, positive changes in the Group 2 occurred earlier and with greater intensity as comparison to the Group 1 in the same time frame. These changes were characterized by an earlier appearance of immature and mature forms of metaplased cells (indicating an increased activity of the epithelium regeneration process), a decreased amount of neutrophils and coccal microflora, decreased evidences of degenerative changes in the epithelial cells and subsequently the earlier increase in the number of epithelial cells, arranged in layers and in the amount of the surface epithelium cells.

Dynamic measurement of the lesion area in patients, carried out for investigation of the reparative effect in the course of different treatment, indicated more pronounced epithelialization in patients of Group 2.

By day 30, Group 1 showed the average area of lesions equal to 3.0±0.2 mm^2, Group 2, 1.5±0.3 mm^2 and the intensity of shift in average lesion area was 60.16 and 75.34% in Group 1 and 2, respectively.

During clinical observation of patients with erosive and ulcerative form of lichen ruber planus we revealed that on day 5 of the treatment of the oral mucosa diseases by platelet autoplasma the patients had no complaints of pain in speaking and eating. We objectively observed the epithelialization of erosive and ulcerative lesions. For example, prior to treatment, the patients of Group 1 and 2 had the average area of the lesions equal to 8.0±0.7 mm^2. On day 7, the value in Group 1 remained the same while in Group 2 decreased up to 3.5±0.7 mm^2 (56.25%). The patients of Group 1 had a decrease in lesion area observed on day 10 equal to 6.0±0.5 mm^2 (25%) and the average value in Group 2 was 0.5 mm^2. The patients of Group 1 had no complete epithelialization observed by the end of the treatment in contrast to the second group. The 1 month after the final treatment, the second group showed the improved results of cytological indicators.

The normalization of oral mucosa epithelium in the lesions area of patients treated with platelet-rich plasma proceeded in a shorter time as evidenced by the data obtained by dynamic cytology as well as measurement values of the lesions area in patients with erosive and ulcerative form (shift in lesion area average by day 30 in this group was 80% while the same in the group having only medical treatment was 60.16%).

Morphological examination of the oral mucosa in control animals allowed us to determine a fragment of mucosa lined with hyperplastic, multilayered, non-squamous epithelium with focal acanthosis and the underlying tissue with focal sclerosis, foci of chronic inflammation represented by an accumulation of lymphocytes, histiocytes and fibroblasts with single gigantic debris-type multi-core cells with areas of maturing granulation tissue.

Histological examination of a fragment of mucosa lined with hyperplastic, multilayered, non-squamous epithelium, conducted on day 14 in Group 2 undergoing autochemotherapy, allowed us to reveal the signs of acanthosis, the underlying tissue with diffuse lymphohistiocytic infiltration with a mixture of neutrophils and a group of newly formed blood vessels. A moderately severe congestion of the blood vessels was observed more often which led to an increase in their diameter, i.e., reparative function has recovered.

Thus, the histological changes in the control group indicate the development of destructive and inflammatory changes in the early stages of the experiment (day 14). The group of animals undergoing platelet autoplasma showed the recovery of histological structure of connective tissue, the reduction of the inflammatory response, the earlier maturation of granulation tissue with increasing amount of fibroblasts, lymphocytes, histiocytes, admixed with neutrophils.

DISCUSSION

Comprehensive treatment of patients with erosive and ulcerative lesions in the oral cavity with the use of Plasmolifting technique has ensured faster, more intensive than under conventional medical treatment normalization of clinical and cytological parameters. Inclusion of autohemotherapy in the treatment regimen of patients with lichen ruber planus of the oral mucosa has contributed to a more pronounced positive dynamic than in case of a conventional medical treatment as well as ensured acceleration of their regeneration.

Based on the morphological study it was found that the use of autohemotherapy ensures a stable regeneration of connective tissue, lymphohistiocytic infiltration, rapid maturation of the granulation tissue which indicates a rather quick repair of the oral mucosa, stimulated processes of tissue regeneration, quickly stopped inflammation and recovery of the reparative function. Activation of the regeneration period of mucosal wound surface ensures, certainly, reduction in the resulted defect due to the intensive formation of new connective tissue consisting of collagen bundles with few cells and blood vessels therebetween.

Thus as a result of our study of clinical criteria in the treatment of erosive and ulcerative lesions of the oral cavity with the use of autohemotherapy it has been proved that the local application of autologous plasma as a part of comprehensive treatment has a positive effect on the clinical progress, reduces the intensity and duration of pain, accelerates mucosal regeneration and reduces the amount of inflammations and necrotic changes. As a result, there is more intensive formation of a resistant granulation tissue and active reduction in defect size.

CONCLUSION

Findings of immediate and long-term results of comprehensive treatment of patients with erosive and ulcerative lesions with the use of platelet plasma indicate its greater efficiency as compared to the conventional method which makes this method of the disease treatment more advantageous.

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