Clinical and Laboratory Analysis of the Effectiveness of Pharmacotherapy of Aphthous Stomatitis

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Abstract

Aphthous stomatitis is one of the most common diseases among pathologies of the oral mucosa throughout the world and in every age group of the population. Etiology and pathogenesis are multifactorial, and treatment issues remain controversial among researchers of this pathology. Only the need for highly effective local treatment is unambiguous, which will improve the quality of life of patients.

The aim of the study was a clinical and laboratory analysis of the effectiveness of various pharmacotherapy agents in the local treatment of aphthous stomatitis. The study involved 60 patients who were divided into 2 groups (conventional topical therapy - group A; ozonized oil solution - group B). The dynamics of the course of aphthous ulcerations was assessed after 3, 7, 14 days on the basis of changes in the diameter of aphthae, pain intensity, semi-quantitative data and a cytological picture.

The results of all research methods proved that the speed of healing and relief of pain syndrome occurs faster when using oleotherapy in combination with ozonation. But this method did not allow to reduce the frequency of relapses of new aphthae in long-term follow-up.

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Introduction

Oral aphthae and aphthae-like ulcerations are one of the most common forms of oral ulceration[1]. The etiology is multifactorial, as is the treatment. Aphthous stomatitis affects 20 to 25% of the population and is one of the most common oral lesions in the general population[2]. In addition, such oral ulcerations may appear secondary to a number of well-defined pathological conditions[3].

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In some cases, such ulcerations are refractory, can persist from several weeks to months and disrupt the patient's normal condition, reducing the quality of life. Treatment of aphthous oral ulcers is a challenge. For oral aphthous stomatitis or recurrent aphthous stomatitis caused by a systemic disease, topical therapy is preferred because of its minimal side effects. Systemic drugs are needed if the disease progresses and are prescribed by a general practitioner[4].

Currently, there is no highly effective specific topical treatment to relieve the symptoms caused by canker sores[5]. The generally accepted treatment strategy is to reduce the pain and duration of the lesions. Topical corticosteroids, antibiotics, and analgesics are strongly recommended in therap.[6] However, longer and

repeated chemical treatments can cause fungal infections and drug resistance, which can lead to more serious side effects and life-threatening complications later on. General recommendations include avoiding solid, acidic and salty foods, as well as alcohol and carbonated drinks[7]. In addition, toothpastes containing sodium lauryl sulfate should not be used. Mouth rinses with chlorhexidine digluconate solution and topical corticosteroids have been shown to reduce the severity and duration of aphthous aphthous stomatitis.[8] However, chlorhexidine bigluconate solution, widely used in commercial oral antiseptics, has shown high cytotoxicity against human fibroblasts and osteoblasts. Use of systemic non-steroidal anti-inflammatory drugs (NSAIDs) or even steroids can have gastrointestinal and cardiac toxicity as well as nephrotoxic side effects[9].

There is a desperate need for new pharmacological molecules that act differently than the chemicals used, but are able to reduce the inflammatory process without side effects for the body, while stimulating wound healing processes[10,11].

Currently, there are many methods of local pharmacotherapy of aphthous lesions. It is very difficult for a dentist to make the right choice when prescribing a particular drug to patients. It is necessary to comprehensively assess the clinical situation, taking into account all factors, including laboratory research[12,13]. Conducting a comparative analysis of the effectiveness of the treatment of aphthous stomatitis was the purpose of this study.

Purpose of the study - to conduct a clinical and laboratory analysis of the effectiveness of pharmacotherapy in the treatment of aphthous stomatitis.

Materials and methods

A randomized controlled trial was conducted among young patients according to WHO (18-44 years old) with a clinical diagnosis of small aphthous stomatitis K12.00 (ICD 10) on the basis of the Department of Dentistry of the Institute Department of Continuing Medical Education and Distance Learning Federal State Budgetary Educational Institution of Higher Education " Volgograd State Medical University" of the Ministry of Health of the Russian Federation and was approved by the local ethical committee of the federal state budgetary educational institution of higher education "Volgograd State Medical University" of the Ministry of Health of the Russian Federation dated March 22, 2021, certificate No. 2021/017. The criterion for inclusion in the study was a clinical diagnosis of small aphthous stomatitis according to the Stanley classification (ulcers less than 10 mm in size, located on non-keratinizing surfaces of the mucous membrane, recurring at intervals of 1-4 months, healing after 7-10 days). The exclusion criteria are: pregnancy, allergic reactions to the drugs used, chronic diseases (eg hepatitis, AIDS, celiac disease, IgA deficiency, diabetes, etc.) and medications (eg antibiotics, antifungals, corticosteroids, hormone therapy and etc.).

The patients were divided in a 1:1 ratio into 2 groups (30 people each): group A, whose patients received the generally accepted treatment regimen in accordance with the recommendations of the national guidelines for therapeutic dentistry edited by L.A. Dmitrieva from 20195 (application anesthesia with 10% lidocaine solution; washing with weak antiseptics of the oral cavity, removing soft plaque from the surface of the mucous membrane of the mouth and teeth; removal of necrotic masses using the enzyme trypsin, 1 mg of which is dissolved in 1 ml of 0.9% sodium solution chloride; adhesive dental paste solcoseryl for 10 minutes 2-3 times a day; imudon (6-8 tablets per day)[5], and group B, the treatment of which also included washing the oral cavity with weak antiseptics, removing soft plaque from the surface of the oral mucosa and teeth; removal of necrotic masses using the enzyme trypsin, 1 mg of which is dissolved in 1 ml of 0.9% sodium chloride solution; and applications with ozonated oil. Informed written consent was obtained from all patients. The study was conducted from April 2021 to April 2022 of the year.

- Aft diameter

[6] Oral aphthous lesions were measured using a device for measuring the size of the affected surface in the oral cavity (Russian Federation patent for utility model No. 166417 diameter assessment (mm)[6]. Evaluation was carried out on day 1 (immediately before the start of treatment), on day 3, on day 7 and on day 14.

- Semi-quantitative data

During a clinical examination, the presence of signs of suppuration, necrotic changes, connective tissue fibrosis, edema, hyperemia was determined (+ - weak; ++ - moderate; +++ - pronounced; - absent).

- Cytological examination

To control the course of the wound process, determine its phase, the effectiveness of the proposed combined method of treatment, a study of cytological prints was carried out. The material was a scraping from the surface of aphthous ulcerations. Previously, the patient rinsed the mouth and removed necrotic masses, then the test material was applied to a glass slide. The material was then dried at room temperature and sent to the laboratory. Under a microscope, the cellular composition was determined, the results were evaluated according to five typical characteristics of cytograms: I. necrotic type - the object consists of detritus and remnants of destroyed neutrophils, massive microflora is extracellular; II. degenerative-inflammatory type - the preparation contains a large number of neutrophils in a state of degeneration and destruction in the form of karyopyknosis and karyorrhexis, cytolysis; III. inflammatory type - neutrophils of an average degree of preservation make up 85-90%, and 5-10% are accounted for by lymphocytes and monocytes, individual macrophages and polyblasts; IV. inflammatory-regenerative type - the number of neutrophils decreases to 60-70%, their safety increases. 20-30% of the cells are tissue undifferentiated polyblasts, fibroblasts, lymphocytes, as well as macrophages, an increase in the number of which up to 5-10% is inherent in the process of wound cleansing. The microflora is observed in a small amount in a state of active phagocytosis; V. regenerative type - the content of neutrophils is 40-50%. Young cells of granulation tissue, pro- and fibroblasts, macrophages, endothelium, polyblasts, and epithelium sharply predominate. Microflora practically q

Thus, I-III types of cytograms corresponded to the first phase of the wound process, IV-V types corresponded to the second and third phases[8].

The obtained data were subjected to statistical analysis using the statistical computer program Statistica, version 13.0 (StatSoft Inc., USA). The suggested minimum sample size was n = 60. The descriptive statistics of the tables are represented by the mean value and its mean error (M±m) and percentage calculation. Student's t-test was used for comparison between variables. The statistical significance of differences $p < 0.05$ was considered significant.

Results

A total of 60 patients (35 women and 25 men) with small aphthous stomatitis were included in the study in accordance with the inclusion criteria. The size of the formations ranged from 5 mm to 8 mm. The affected areas of the oral cavity were: upper and lower lip, buccal mucosa, tongue and soft palate. The number of lesions and pre-treatment lesion diameters were similar for the two treatment groups. (p >0,05).

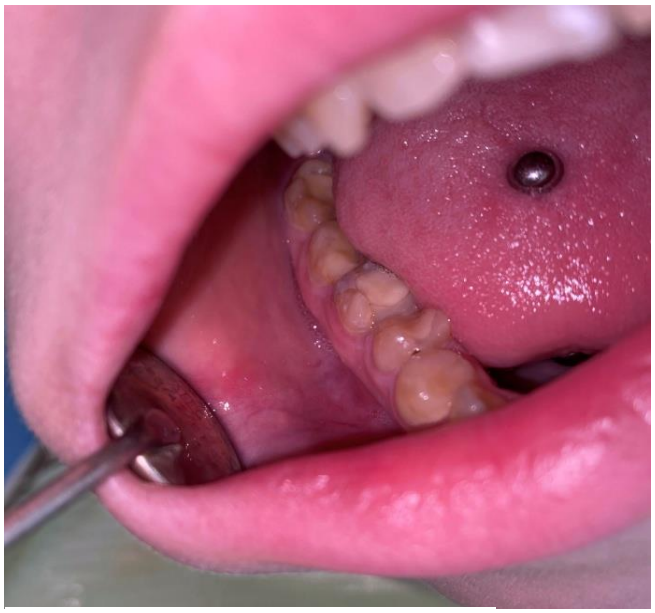


Figure 1a. Afta before treatment.

- Diameter aft

Before treatment, the average lesion diameter was 7.33±0.22 mm in group A and 7.20±0.25 mm in group B (Fig. 1a). On the third day, the mean diameter decreased to 4.33±0.3 mm in group A and 4.28±0.2 mm in group B; after seven days, the mean value was 3.18 ± 0.1 mm in group A and 2.98 ± 0.1 mm in group B. Both groups showed a progressive decrease in the length of aphthae with complete healing on day 14 (Fig. 1b) . The difference in ulcer diameter reduction between the two groups was statistically significant at day 7. (Table)

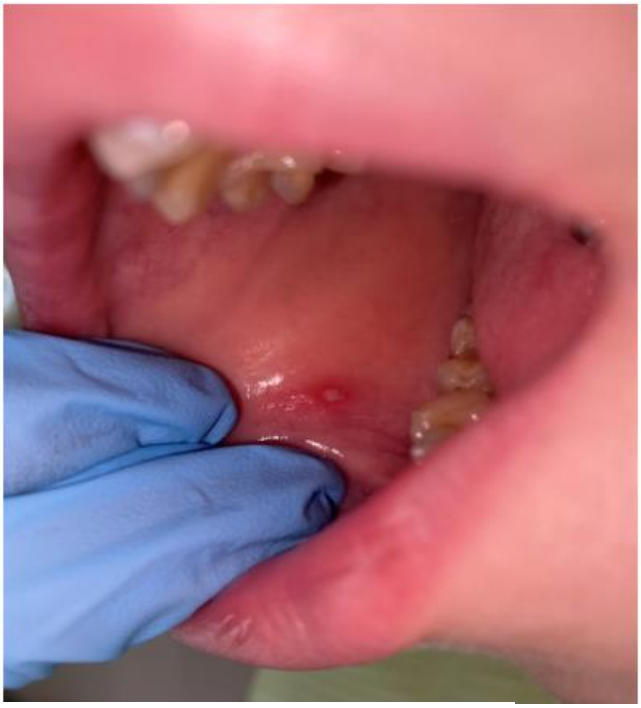


Figure 1b. After 14 days, complete epithelialization.

	Group A	Group Б
Before treatment	7,33±0,22 mm	7,20±0,25 mm
3 days	4,33±0,3 mm	4,28±0,2 mm
7 days	3,18 ± 0,1 mm*	2,98 ± 0,1 mm*

Table 1. Dynamics of aft healing during the week.
Note: * - statistical significance between groups p<0,05.

Pain assessment

Before the start of treatment, patients of both groups noted severe pain, aggravated by eating, talking, and the pain intensity index was 4.1±.07 points in group A and 4.2±0.9 points in group B. After 3 days, patients in group B noted a significant decrease in pain intensity and the indicator was at the level of 2.0±0.1 points, which is 1.5 times less than in group A, where it was 3.0±0.3 points. On the 7th day, the intensity of pain in both groups was insignificant and amounted to 1.0±0.21 points in group A, and 1.0±0.2 points in group B. A statistically significant difference in pain reduction between the two groups was observed only on day 3 (p<0.05) (Figure 2). After 14 days from the start of treatment, there was no pain.

- Semi-quantitative data

Clinical examination showed no signs of suppuration, necrotic changes, connective tissue fibrosis. The indicators of semi-quantitative data are presented in Table 2 below.

Signs	Before treatment		3 days		7 days		14 days	
	Gr.A	Gr.B	Gr.A	Gr.B	Gr.A	Gr.B	Gr.A	Gr.B
Edema	+++	+++	++	++	+	+	-	-
Hyperemia	+++	+++	++	++	+	+	-	-

Table 2. Dynamics of semi-quantitative changes.
Note: + - weak; ++ - moderate; +++ - expressed; - missing.

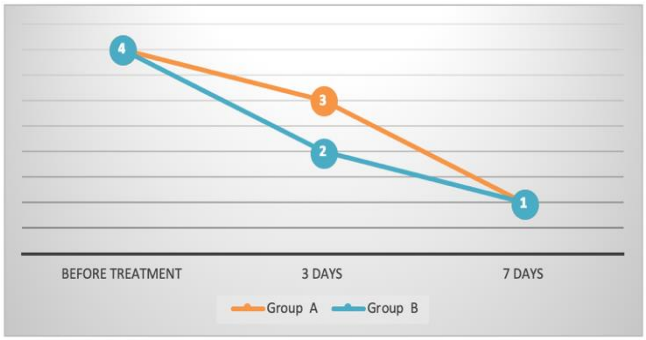


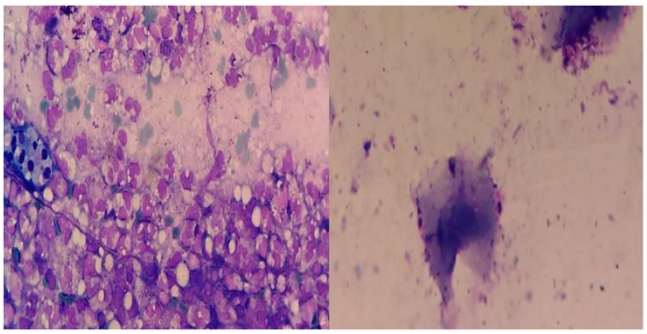
Figure 2. Pain intensity scale VAS.

- Cytological examination

At the time of the examination of patients before the start of treatment, in the cytograms of smears-imprints of both groups, the picture of acute inflammation prevailed and corresponded to the necrotic and degenerative-inflammatory type: against the background of erythrocytes, leukocytes (neutrophils are single intact and dilapidated), fibrin filaments, nuclei of destroyed cells, single cells of squamous epithelium , fibrin threads, a large number of cocci, nuclei of destroyed cells (Fig. 3a).

On the 3rd day, the pattern of cytograms of patients in group A began to correspond to the degenerative-inflammatory and inflammatory type in the ratio of 25:5, and in group B this ratio of cytograms of patients was 20:10, which corresponds to the first phase of the wound process, but type III of cytograms in group B occurs 2 times more often than in patients of group A.

After 7 days of therapy, the cytological picture of patients in group A corresponded to the inflammatory-regenerative and regenerative type of cytograms in a ratio of 24:6, and in group B this ratio was 18:12. This result corresponds to phases II-III of the wound process; neutrophils, fibroblasts, macrophages, and epithelium are found in the imprint smears (Fig. 3b). In patients of the group, the predominance of V-type cytograms is observed 2 times more often than in group A.



a **b**

Figure 3a, b. Cytogram of a smear-imprint from the surface of an aphtha. A Before treatment Mallory staining. Initial magnification x50. B Day 7 Stained with hematoxylin and eosin. Initial magnification x100.

On day 14, patients in both groups showed complete epithelialization.

Discussion

The present study evaluated the effectiveness of the use of an ozonated oil solution in the topical treatment of aphthous stomatitis, both in terms of pain relief, and reduction in the size of the lesions and the speed of the onset of the phases of the wound process. According to our results, the use of the method of ozonation and oleotherapy made it possible to statistically significantly reduce the diameter of the ulcer on the 7th day of pharmacotherapy.

According to our results, oleotherapy combined with ozonation in the treatment of aphthous stomatitis leads to a significant reduction in pain after three days of therapy. In addition, it is necessary to note the advantage of this method of treatment relative to the generally accepted scheme in the ergonomics of medical manipulations, the use of a pre-ozonized oil solution can reduce the number of applications of various pharmacological agents.

A cytological study shows that the use of an ozonized oil solution can accelerate the change in the phases of the wound process, which proves the results of previous studies and the high efficiency of the proposed method in reducing the period of exacerbation of aphthous stomatitis.

Conclusions

Long-term results after 6 and 12 months showed that oleotherapy did not reduce the frequency of relapses of aphthous stomatitis in patients, therefore, despite the fact that the etiology and pathogenesis of aphthous stomatitis remain controversial issues, it is necessary to search for means and methods that can influence the increase in the period of remission of this diseases.

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Declaration of Interest

The authors report no conflicts of interest pertaining to any of the products or companies discussed in this article.

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