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Use and Effectiveness of Ozone in the Complex Treatment of Chronic Recurrent Aphthous Stomatitis in Patients with Chronic Gastroduodenitis

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Abstract **Objective:** to increase the effectiveness of treatment of chronic recurrent aphthous stomatitis of the oral mucosa against the background of chronic gastroduodenitis by correcting dysbiotic disorders and enhancing antioxidant protection through pathogenetic therapy. **Methods:** general clinical, laboratory, biochemical, functional, instrumental and statistical methods were used in the course of the study. **Results obtained:** Clinical studies in patients with chronic recurrent aphthous stomatitis of the oral mucosa against the background of chronic gastroduodenitis have shown: a decrease in the following indicators by 1.24 times, a deterioration in hygiene by 1.92 times, an increase in the Schiller-Pisarev test by 2.06 times, an increase in stimulated salivation by 1.84 times and the absence of stimulated salivation by 2.09 times, a shift in The pH is in the acidic side. **Conclusions:** The results of clinical and laboratory studies during operative and long-term follow-up showed that the therapeutic and prophylactic complex developed by us for the treatment of oral mucosal diseases in chronic gastroduodenitis has a long-term bactericidal effect against pathological microbes. The local immune status of the oral cavity was observed to approach the norm.

Keywords Chronic recurrent aphthous stomatitis, Dental caries, Periodontal diseases, Epidemiological study, Chronic aphthous stomatitis, Oral mucosa

1. Introduction

It has been proven that in patients with chronic gastroduodenitis, the composition of the microflora changes and the activity of intestinal enzymes is altered. As a result of the disruption of normomicrobiosis, intestinal dysbiosis develops in the body, accompanied by both qualitative and quantitative changes in the permanent representatives of the oral microflora and a restructuring of the oral biocenosis. This leads to a decrease in the body's nonspecific resistance and antioxidant protection, causes infectious and inflammatory processes in the oral mucosa, and increases the progression of diseases in it.

Many authors note that dysbiotic diseases occur along with suppression of the obligatory normal flora, creating conditions for the growth and colonization of coagulase-negative staphylococci, non-hemolytic streptococci, lactobacilli, corynebacteria, aerobic gram-negative bacilli (non-pathogenic fungi), and neisseriae. The prolonged persistence of the above-mentioned pathogenic microflora in the oral mucosa leads to the development of chronic recurrent aphthous stomatitis (CRAS).

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In the last decade, the incidence of oral mucosal diseases has increased by more than 30%, and the incidence of chronic stomatitis has risen to 60%. Due to the high variability and constant adaptation of microflora, the irrational selection of antibacterial therapy, and the high level of adaptation to the components of antifungal drugs, there has been an increase in the number of relapses of lesions that are difficult to treat with traditional methods, which significantly worsens patients' quality of life.

The above indicates the need to improve diagnostic methods, search for new means for the treatment and prevention of chronic recurrent aphthous stomatitis of the oral mucosa, and apply modern treatment methods based on the pathogenetic mechanisms of such lesions.

The various exogenous and endogenous causative factors of different diseases of the oral mucosa act as chronic, long-term stress agents that lead to disturbances in cellular adaptation ("distress") through a nonspecific reaction of inhibiting biologically active substrates, in particular respiratory enzymes and functionally related ultrastructures.

Recent scientific studies have shown that damage to teeth and oral mucosal tissues occurs alongside inflammatory diseases characteristic of the gastrointestinal tract. This suggests that the pathology of the dentoalveolar system is not only of local nature but is also associated with a significant

systemic response of the whole body.

At present, one of the main directions of research in dentistry is to establish possible relationships between oral pathologies and systemic diseases, as well as between regional homeostasis of the oral cavity and the general homeostasis of the body. Therefore, a comprehensive approach to the medical treatment of periodontal diseases is increasingly being recognized.

Despite the achievements of modern dentistry, the issue of developing an effective and widely applicable method for treating oral mucosal diseases, including chronic recurrent aphthous stomatitis, has not been fully resolved and continues to remain relevant and socially significant.

Taking into account modern concepts about the etiology of oral mucosal lesions, the main directions of therapy should include: local anti-inflammatory therapy; general and local therapy considering the presence of chronic gastroduodenitis; and a pathogenetically oriented approach.

Research aim: To increase the effectiveness of treatment for chronic recurrent aphthous stomatitis in patients with chronic gastroduodenitis by improving dysbiotic conditions of the oral cavity and enhancing antioxidant protection through pathogenetic therapy.

2. Research Materials and Methods

To accomplish the tasks, we used comprehensive research methods. The object of the study was the clinical features of the disease course in patients with chronic gastroduodenitis, biochemical indicators of unstimulated oral fluid, and microbiological changes in CRAS. To achieve the set goal, 118 patients aged 24 to 56 years were examined: 70 men and 48 women. The clinical study involved 118 individuals (Table 1). Among them, 34 were practically healthy without somatic pathology, and 84 were patients with chronic gastroduodenitis. In accordance with ICD-10, the diagnosis of “gastritis and duodenitis” (code K29) and unspecified gastroduodenitis (code K29.9) was made by gastroenterologists of the gastroenterology department.

Table 1. Distribution of Patients by Age and Sex

Age groups	Gender			
	Man		Woman	
	Abs.	%	Abs.	%
24–29 years old	4	5.71	3	6.25
30-35 years old	9	12.86	6	12.50
36-40 years old	6	8.57	4	8.33
41-45 years old	16	22.86	12	25.00
46-50 years old	13	18.57	8	16.67
51-56 years old	22	31.43	15	31.25
Total	70	100	48	100

The first (main) group consisted of 46 individuals (25 men and 21 women) suffering from chronic recurrent aphthous stomatitis of the oral cavity and chronic gastroduodenitis. In the treatment of chronic recurrent aphthous stomatitis, the traditional therapeutic approach was applied, namely local anesthesia, antiseptic treatment, antiviral, antibacterial, and antifungal agents, as well as keratoplastic agents.

For the treatment of chronic recurrent aphthous stomatitis in patients with chronic gastroduodenitis, in addition to the traditional treatment, a special therapeutic algorithm was developed (Figure 1). One of the modern and scientifically proven theories is the immunological concept of the pathogenesis of this pathology. Therefore, the priority direction in the treatment of CRAS is immunomodulatory therapy.

One of the immunomodulation methods is to enhance the immune system using lipopolysaccharides of bacterial origin. A medicinal product containing bacterial lysates is **Imunal**.

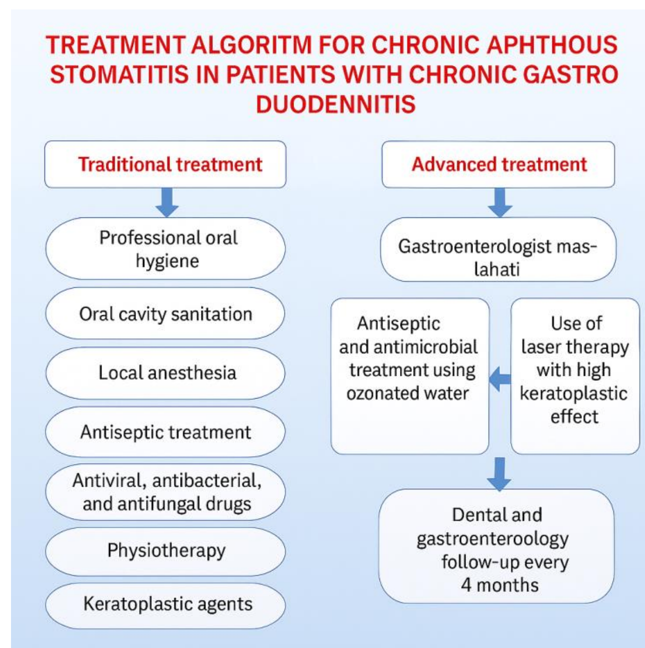

Figure 1. Structure of the Special Treatment Algorithm for Chronic Recurrent Aphthous Stomatitis in Patients with Chronic Gastroduodenitis

The second (comparison group) consisted of 38 patients (24 men and 14 women) with chronic recurrent aphthous stomatitis of the oral cavity and chronic gastroduodenitis, who were treated according to the generally accepted (traditional therapy) standards. Patients in both the main group and the comparison group were required to repeat the treatment course after 6 months.

The third (control group) included 34 individuals (21 men and 13 women) without somatic pathology. Examination data and treatment course information were recorded in the patient’s personal medical record. The effectiveness of treatment was assessed 14 and 30 days after therapy based on clinical outcomes, biochemical, and microbiological indicators. Long-term results were evaluated after a 12-month follow-up period.

Ozone, as a disinfectant, has several advantages over other substances:

Ozone is an extremely powerful disinfectant capable of neutralizing 99.9% of pathogenic microorganisms.

It reacts faster than other antiseptic substances.

Due to the size of ozone molecules being 150% smaller than the molecules in other liquid antiseptics, it is capable of penetrating nanostructures.

The local use of an ozono-oxygen solution generated by the Prozone device, which has high clinical efficacy, significantly reduced the need for certain medicinal products associated with adverse effects and made it possible to completely eliminate subsequent relapses (Figure 1).

In recent years, accumulated clinical experience has shown that the pathology of the oral cavity organs and tissues can only be halted by therapeutic measures, but cannot be completely cured. In this regard, it is necessary to develop and widely implement preventive measures for major dental diseases and to understand the patterns of functioning of a healthy body.

Diseases of the oral mucosa, which often progress with chronic and periodic remissions and exacerbations, arise against the background of an acquired secondary immunodeficiency state. One of the modern and scientifically proven theories is the immunological concept of the pathogenesis of this pathology.

Therefore, the priority direction in the treatment of CRAS is immunomodulatory therapy. One method of immunomodulation is strengthening the immune system with bacterial lipopolysaccharides. A medicinal product containing bacterial lysates is Imunal.

3. Results

The findings of the clinical examination were confirmed by biochemical studies. Fourteen days after the application of the therapeutic–preventive complex in the main group, analysis of the changes in indicators showed a 1.81-fold decrease in elastase activity ($p < 0.05$) and a 1.56-fold decrease in MDA concentration. Ozonated water and *Imunal*, which have anti-inflammatory effects, prevent the accumulation of lipid peroxidation products in the oral cavity.

A marked increase in MDA concentration, which is an indicator of lipid peroxidation processes, completely disappeared in the main group 30 days after the comprehensive treatment. A significant reduction in the severity of inflammatory signs was observed: the content of the proteolytic enzyme elastase decreased 2.53-fold ($p < 0.02$) and MDA decreased 2.15-fold ($p < 0.05$), almost reaching normal values.

Long-term results after one year of follow-up in the main group showed that elastase activity decreased 2.0-fold ($p < 0.02$) and MDA levels decreased 1.87-fold ($p < 0.05$), which corresponded to normal values.

In the comparison group, after 14 days, elastase activity and MDA concentration decreased 1.17-fold, remaining at a high level. A significant reduction in the severity of inflammatory signs was observed after 30 days — elastase decreased 1.94-fold and MDA decreased 2.0-fold ($p < 0.05$).

The results of studies conducted after one year in the comparison group showed only a short-term effect of treatment using the standard method. The LPO indicator did not reach normal levels: MDA levels changed insignificantly — a 1.12-fold decrease, remaining significantly higher than in the main group, and elastase activity decreased only slightly — 1.21-fold.

The state of the body's peroxidation processes and antioxidant systems was monitored more precisely before treatment and one month later by tracking the dynamics of the API. In the main observation group, 30 days after treatment, the activity of the antioxidant enzyme catalase increased significantly—by 3.0 times ($p < 0.01$)—approaching normal values as closely as possible. In the comparison group, treatment had no significant effect on this enzyme, with activity increasing only 1.67 times ($p < 0.02$). The API index, calculated based on MDA and catalase measurements, showed a marked upward trend in patients of the main group—by 6.96 times ($p < 0.001$)—whereas in the comparison group, the API index increased only slightly—by 2.18 times ($p < 0.001$).

One year after treatment, a biochemical study of unstimulated oral fluid in patients of the main group revealed positive trends. The use of "ozonated water" (as a rinse and orally) led to a 2.75-fold increase in catalase activity ($p < 0.01$) and a 6.21-fold increase in the API index ($p < 0.001$), values consistent with those of healthy individuals.

The pronounced antioxidant properties of the dietary concentrate help normalize the antioxidant–prooxidant system and demonstrate its long-term effect.

The obtained long-term results confirm the ability of "ozonated water" to prevent pathological processes in the oral cavity caused by prolonged elevated lipid peroxide levels. After one year of observation, the degree of dysbiosis in patients of the main group decreased by 3.06 times ($p < 0.01$), indicating a beneficial effect of therapeutic and preventive agents on the oral microbiocenosis. In the comparison group, DD decreased only 1.28 times compared with the initial state, suggesting a reduction in the protective function of the oral cavity, deterioration of local immunity, and weakening of the body's defenses, which contribute to increased growth of opportunistic microorganisms in the oral cavity, microbial proliferation, and the complication of the clinical course of chronic stomatitis.

Table 2. Indicators of the Level of the Biochemical Marker of Inflammation (Elastase) in Unstimulated Saliva after Treatment, mkat/L (M±м)

№	Observation group	n	Before treatment	After 14 days	After 30 days	After 1 year
1.	Main	46	0,38±0,06	0,21±0,004*	0,15±0,005**	0,19±0,006**
2.	Comparison group	38	0,35±0,08	0,30±0,007	0,18±0,006*	0,29±0,003

The recommended "ozonated water" rinse and Immunal halt the process of microbial colonization. They can be used for oral cavity treatment to prevent colonization by Candida, as well as the formation of bacterial–fungal associations.

The study results showed that the use of our recommended complex for the treatment and prevention of candidal lesions of the oral cavity suppresses fungal growth, prevents the recurrence of chronic forms of candidiasis, and inhibits exacerbations of this disease.

In the study of microbial contamination of the oral cavity in patients with chronic gastroduodenitis, a heterogeneous microbial composition of the oral cavity was identified. In these patients, *Staphylococcus epidermidis* strains were detected in 38.9% of cases, *Enterococcus* strains in 16.7%, and *Staphylococcus aureus* strains in 5.5%. In the oral cavity of patients with chronic gastroduodenitis, *Staphylococcus epidermidis* strains predominated (33.3%), while *Streptococcus haemolyticus* strains were also detected (5.5%). In all patients with chronic hepatitis B and C, the oral microflora was dominated by *Staphylococcus epidermidis* strains.

When complex therapy with immunomodulators was performed, patients in the main group demonstrated a positive clinical effect, manifested by the cessation of aphthae formation by day 2 of treatment, and their complete disappearance by day 4. In the control group, similar changes occurred significantly later—on days 8–10. At 20 days and 6 months after treatment for chronic recurrent aphthous stomatitis (CRAS), a good oral hygiene index (according to Fedorov–Volodkina) was recorded in the main group. In contrast, patients in the control group showed unstable clinical results and increased key indicators pointing to disease progression.

In patients with chronic gastroduodenitis, the use of a special treatment algorithm—comprising ozonated water, laser therapy, and Immunal—resulted in an increase in the initially low relative counts of T-lymphocytes and the T-helper subpopulation, approaching those observed in healthy individuals. This specialized treatment improved the immunological parameters of patients with chronic gastroduodenitis.

Various degrees of inflammatory and dystrophic changes were observed in the oral mucosa and periodontal tissues, with severity depending on the type of virus, viral load, and activity of pathological processes in the gastrointestinal tract.

Thus, in CRAS, the underlying mechanisms include disturbances in the immune status of the mucosa, accumulation of peroxidation products and inflammatory elements, hypoxia, dystrophy, and destruction of mucosal tissues.

4. Conclusions

Clinical studies in patients with chronic recurrent aphthous stomatitis (CRAS) on the background of chronic gastroduodenitis showed the following changes: a 1.24-fold decrease in certain clinical parameters, a 1.92-fold worsening of oral hygiene, a 2.06-fold increase in the Schiller–Pisariev test results, a 1.84-fold reduction in stimulated salivary flow, a 2.09-fold reduction in unstimulated salivary flow, and a shift of pH toward acidity.

Biochemical examination of stimulated oral fluid in patients with chronic gastroduodenitis revealed a marked increase in the activity of inflammatory markers: elastase increased 3.45-fold and malondialdehyde (MDA) 1.87-fold. At the same time, the activity of the antioxidant enzyme catalase decreased 3.5-fold, and the reduction of the Antioxidant–Prooxidant Index (API) by 6.25-fold reflected significant changes in the antioxidant–prooxidant balance.

The therapeutic measures we propose normalize MDA, elastase, and catalase activity, restore antioxidant defense, significantly reduce urease levels, increase lysozyme secretion, and contribute to the normalization of the oral microbiocenosis.

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