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ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

CLINICAL AND LABORATORY FEATURES OF DISEASES OF THE ORAL MUCOSA OCCURRING AGAINST THE BACKGROUND OF GASTRIC AND DUODENAL ULCER AND IMPROVEMENT OF THEIR TREATMENT

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GENERAL CHARACTERISTICS OF THE WORK

Relevance and degree of development of the topic. A relationship has been established between diseases of various organs and systems of the body and a number of pathological processes observed in the oral cavity.[1]

Numerous studies have shown that the association between diseases of the gastrointestinal tract (GIT) and chronic recurrent aphthous stomatitis is related to metabolic disorders as well as immunological and biochemical changes.[2,3]

Chronic recurrent aphthous stomatitis (CRAS) is a chronic inflammatory disease characterized by the formation of painful aphthae on the oral mucosa and may recur with varying frequency.[4] According to the World Health Organization, CRAS occurs in every fifth inhabitant of the planet.[5] The prevalence of CRAS ranges from 3.6% to 60%, depending on geographical characteristics.[6]

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Current studies have shown that the incidence of recurrent aphthous stomatitis in inflammatory diseases of the gastrointestinal tract increases to 11.6%, and in some cases to 40–50%. According to several studies, the proportion of CRAS in the structure of oral mucosal diseases ranges from 4.68% to 9.3%.[7]

Many authors note that the frequency of Chronic recurrent aphthous stomatitis in combination with inflammatory gastrointestinal diseases increases to 40–50%. Gastrointestinal tract pathologies occupy a leading place in the etiology of Chronic recurrent aphthous stomatitis.[8] Gastritis and gastric and duodenal ulcers are observed in 60% of patients with CRAS. Chronic diseases of the digestive system (gastritis, ulcer) are accompanied by deficiencies of vitamins, minerals, proteins and carbohydrates and by impaired immunity.[9] These changes contribute to the development of functional and organic disorders and chronic disease of the oral mucosa.[10]

This disease is accompanied by deterioration of the general condition of the body; the physiological process of food intake is disturbed, body temperature often rises, and lymph nodes enlarge. With timely treatment, the disease lasts 7–10 days. At the same time, the presence of concomitant diseases and weakened immunity contributes to exacerbation of the process (recurrences) and transition of the disease to a chronic form.

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Based on the data obtained on the condition of the oral mucosa and dental status in patients with gastrointestinal diseases, as well as on the dynamic assessment of non-specific resistance of the oral cavity and biochemical parameters of oral fluid, it may be concluded that the most effective comprehensive therapy for Chronic recurrent aphthous stomatitis includes drugs with antioxidant properties and sorbents in the local treatment regimen.

Object and subject of the study. The study included 131 patients with gastrointestinal tract pathology and diseases of the oral mucosa. Their clinical characteristics, laboratory findings and treatment outcomes constituted the subject of the study.

Aim of the study. To evaluate, using clinical, biochemical and immunological methods, the effectiveness of comprehensive treatment (sorbent and antioxidants) in patients with chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer.

Objectives of the study:

1. To determine the main clinical manifestations of the oral mucosa and dental status in patients with gastrointestinal pathologies.
2. To determine the frequency of different severity grades of chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer.
3. To study antioxidant and enzymatic activity, cytomorphological parameters, protein levels and the state of non-specific immunity in oral fluid in different severity grades of chronic recurrent aphthous stomatitis.
4. To evaluate the clinical effectiveness of comprehensive treatment based on the combined use of a sorbent and an antioxidant.
5. To evaluate the effect of comprehensive treatment on antioxidant and enzymatic activity in oral fluid and on indicators of non-specific immunity of the oral cavity.

Research methods: clinical methods included history taking, examination, assessment of primary and secondary lesion elements, and stomatoscopy. Laboratory methods included cytomorphological examination of the oral cavity and determination of biochemical

parameters: protein level in oral fluid, activity of the antioxidant system, enzyme levels, and statistical analysis.

Main provisions submitted for defense:

– Among oral mucosal lesions in patients with gastric and duodenal ulcer, chronic recurrent aphthous stomatitis was encountered predominantly in mild and moderate forms. The dental status of patients with Chronic recurrent aphthous stomatitis was characterized by a high intensity of dental caries, mild gingivitis and an unsatisfactory level of oral hygiene.

– Changes in the level of secondary antioxidants in oral fluid were identified in patients with Chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer; their assessment during treatment made it possible to characterize the state of the antioxidant defense system of the oral cavity.

– Addition of a sorbent and an antioxidant to the comprehensive treatment of patients with Chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer increased clinical effectiveness, shortened the epithelialization time of aphthae, reduced the frequency of recurrences and prolonged the duration of remission.

– Comprehensive treatment involving the combined administration of a sorbent and an antioxidant had a positive effect on non-specific immunity, strengthened antioxidant defense of the oral cavity and normalized enzymatic parameters in patients with Chronic recurrent aphthous stomatitis.

Scientific novelty of the study:

– In patients with Chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer, clinical features, the antioxidant defense system of the oral cavity, and immune and biochemical parameters were comprehensively evaluated, and their relationship with disease severity and clinical course was determined;

– The rationale for the combined use of a sorbent and an antioxidant in the comprehensive treatment of Chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer was substantiated on the basis of the dynamics of clinical, immunological and biochemical parameters;

– Positive clinical outcomes characterized by accelerated epithelialization of aphthous lesions, reduced recurrence frequency and prolonged remission were established after comprehensive treatment.

Practical significance of the study:

– Based on the results of the clinical, biochemical and immunological studies, a comprehensive treatment method involving the combined use of a sorbent and an antioxidant was proposed for chronic recurrent aphthous stomatitis.

– Comprehensive treatment (sorbent + antioxidant), through a local effect on the epithelialization of aphthous lesions, accelerates healing, reduces the intensity of pain syndrome, prolongs remission and decreases the number of disease recurrences.

Approbation. The results of the dissertation were discussed at the following conferences: the International Scientific and Practical Conference "Science and Education in the 21st Century" (Tambov, 2020); the XVIII International Euroasian Congress of Surgery and Hepatogastroenterology (Baku, 2019); the International Scientific Forum "Science and Innovation – Modern Concepts" (Moscow, 2020); scientific-practical conferences dedicated to the birthday of H. Aliyev (Baku, 2022, 2024); scientific-practical conferences dedicated to the anniversary of A. Aliyev (Baku, 2018, 2019, 2021, 2024, 2025, 2026); the International Scientific-Practical Congress "Current Problems of Medicine" dedicated to the 100th anniversary of T. Əliyev (Baku, 2021); the scientific-practical conference dedicated to the 100th anniversary of Academician Zarifa xanım Aliyeva (Baku, 2023); the Medical Festival dedicated to the 102nd anniversary of the birth of the National Leader H. Aliyev and the 95th anniversary of Azerbaijan Medical University (Baku, 2025); the scientific-practical conference dedicated to the 90th anniversary of the Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev (Baku, 2025); and the "International Congress on Dentistry and Oral Health Research" (Ankara, 2026).

The preliminary discussion of the dissertation was held at a joint meeting of the staff of the Departments of Dentistry and Maxillofacial

Surgery, Orthodontics, Therapy, and the Central Scientific Research Laboratory of the Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev (07.11.2024, Protocol No. 13). The study results were presented and discussed at the Scientific Seminar in specialty 3226.01 – "Dentistry" operating under the ED 2.50 Dissertation Council of Azerbaijan Medical University (19.06.2025, Protocol No. 14), and at the Scientific Seminar in specialty 3226.01 – "Dentistry" operating under the FD 2.53 Dissertation Council (10.06.2026, Protocol No. 2).

Application of the research results to practice. The results of the dissertation were incorporated into the curriculum of the Department of Dentistry and Maxillofacial Surgery and used in the training of residents and in continuing professional development courses for dentists. Clinical studies were conducted at the Department of Dentistry and Maxillofacial Surgery of the Azerbaijan State Advanced Training Institute for Doctors named after A.Aliyev, the Gastroenterology Department of the Republican Clinical Hospital named after Academician Mirgasimov, and City Clinical Hospital No. 3.

Published works. The results and fragments of the dissertation have been reflected in 31 scientific works, including 7 articles (2 published abroad) and 21 abstracts (7 published abroad).

Name of the institution where the dissertation was performed. Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev.

Volume and structure of the dissertation. The dissertation consists of an introduction (11307 characters), a literature review (Chapter I, 77,135 characters), materials and methods of the study (Chapter II, 29,243 characters), three chapters presenting the results of the author's own observations (Chapter III, 33,103 characters; Chapter IV, 23,098 characters; Chapter V, 21,597 characters), a general discussion (19,271 characters), conclusions (1,722 characters), practical recommendations (1,272 characters), and a list of references. The bibliography contains 36 sources in Azerbaijani, 112 in Russian, and 45 in English. The dissertation comprises a total of 170 typed pages and includes 39 tables, 21 charts, and 6 figures.

The total volume of the dissertation in characters (excluding spaces, tables, figures and references) is 217,748 characters.

MATERIALS AND METHODS OF THE STUDY

The study included 131 patients with gastrointestinal tract pathologies and diseases of the oral mucosa.

The study was conducted in two stages:

1 – investigation of the clinical and laboratory features of oral mucosal diseases in patients with gastrointestinal tract pathologies;

2 – staged analysis and evaluation of the effectiveness of the proposed treatment regimen using a combination of sorbent and antioxidant preparations in patients with clinical signs of chronic recurrent aphthous stomatitis.

The duration of participation in the study was 12 months, with repeated examinations on days 3, 5 and 7 of the disease and then after 3, 6 and 12 months. The control group consisted of 10 sanitized patients without oral mucosal disease, with a DMFT index not exceeding 4 and without chronic gastrointestinal disease.

The mean age of the examined patients was 49.3 ± 1.4 years. There were 89 men (67.9%) and 42 women (32.1%).

Inclusion criterion: patients with oral mucosal and gastrointestinal pathologies. Exclusion criteria: 1) type I or type II diabetes mellitus, allergic or infectious diseases; 2) pregnancy and lactation; 3) neoplastic disease; 4) mental illness.

During studies conducted from 2018 to 2019, 52 patients with clinical signs of chronic recurrent aphthous stomatitis were identified among patients with gastrointestinal tract pathologies. The clinical presentation of chronic recurrent aphthous stomatitis in the oral cavity varied. The main lesion of the oral mucosa was an aphthous erosion of various shapes, covered with fibrinous plaque, ranging from 1–5 mm to 1–2.5 cm. Aphthae were surrounded by a hyperemic inflammatory halo and could be single or multiple. They were localized on the mucosa of the oral vestibule, the tongue, and the upper and lower lips. Most often, aphthae were located on the lateral surfaces of the tongue

and along the occlusal line of the teeth in the buccal region. Analysis of the clinical course of chronic recurrent aphthous stomatitis made it possible to distinguish two severity grades:

1) Mild CRAS was detected in 32 patients. Their general condition was satisfactory, body temperature was within the normal range, and there were no signs of systemic intoxication. One or two isolated, mildly painful aphthous lesions were observed in the oral cavity.

2) Moderate CRAS was detected in 20 patients. Their general condition was satisfactory; body temperature was subfebrile (37.0–37.5°C). Regional lymph nodes were painful on palpation. Up to three isolated aphthous lesions were recorded in the oral cavity and were painful on palpation. Recurrences occurred 3–4 times per year, and epithelialization of aphthous lesions proceeded at a moderate rate.

Statistical methods. Statistical processing of the obtained indicators was performed using Microsoft Office Excel 2010. Numerical data were presented as the arithmetic mean (M) and standard error of the mean (m). The probability of differences between groups was calculated using the U criterion (Wilcoxon–Mann–Whitney test) (P). Differences were considered statistically significant at $p \leq 0.05$, highly significant at $p \leq 0.01$, and non-significant at $p > 0.05$.

RESULTS OF THE STUDY AND THEIR DISCUSSION

During examination of 52 patients with gastrointestinal tract pathologies, oral mucosal pathology chronic recurrent aphthous stomatitis was identified. The patients were divided into two groups: Group 1 (control) included 23 patients, and Group 2 (main group) included 29 patients with chronic recurrent aphthous stomatitis. Both groups received comprehensive etiopathogenetic treatment. Somatic pathology was managed by a gastroenterologist according to standard treatment protocols, including systemic medications selected with regard to the individual clinical characteristics of each patient. General etiopathogenetic treatment was performed taking into account clinical indicators and individual patient characteristics. For H. pylori eradication, the following regimen was used: rabeprazole 20 mg twice

daily; amoxicillin 1000 mg twice daily; clarithromycin 500 mg twice daily for 10 days. To support the intestinal microbiota, Bifiform was prescribed at 2 capsules twice daily for 2 weeks, followed by 1 capsule twice daily for an additional 2 weeks.

During the study, as part of local therapy in both patient groups, chronic foci of oral infection were eliminated, professional oral hygiene was performed, patients were instructed in individual oral hygiene, and subsequent tooth cleaning was monitored.

There are many different methods and medications for treating chronic recurrent aphthous stomatitis. Antioxidants are successfully used in comprehensive chronic recurrent aphthous stomatitis therapy, while only isolated studies have investigated medical sorbents. Nevertheless, the problem of chronic recurrent aphthous stomatitis treatment remains relevant.Depending on the treatment method, patients with chronic recurrent aphthous stomatitis were divided into two groups: Group 1 (23 patients), in which drug treatment included a conventional therapeutic regimen; and Group 2 (29 patients), in which drug therapy included conventional treatment plus local application of an antioxidant and a sorbent to affected areas of the oral mucosa.

All patients received conventional comprehensive treatment, including elimination of traumatic factors, administration of antiseptic agents and use of agents promoting epithelialization. After antiseptic treatment, patients in Group 2 received topical application of the medical sorbent “Enterosgel” (Russia) to the lesion. The procedure was performed 2–3 times daily for 20–30 minutes until complete epithelialization of the lesions. In addition, patients in Group 2 received the antioxidant preparation “Alligat” (United Kingdom), administered 20–30 minutes after application of Enterosgel.

Depending on the treatment methods used, patients with chronic recurrent aphthous stomatitis and gastrointestinal pathologies were divided into two groups: Group 1 (control, n=23), in which drug therapy included conventional treatment (local anesthesia, antihistamines, antiseptics, epithelializing agents, etc.); and Group 2 (main, n=29), in which drug therapy included conventional treatment

as well as topical sorbent and antioxidant application to affected areas of the oral mucosa. Treatment effectiveness was assessed at the following observation periods: up to 7 days, up to 6 months, and long-term up to 1 year. The criteria evaluated were reduction and complete relief of pain, the rate of epithelialization of aphthous lesions, and the number of recurrences up to 6 months and 1 year. A therapeutic effect was observed in all patients with chronic recurrent aphthous stomatitis. Clinical improvement was manifested by reduced inflammatory intensity, active epithelialization of lesions, decreased pain and discomfort, and reduced severity of intoxication. Pain sensitivity was assessed before treatment and on days 3 and 5 using a pain rating scale. In the control group, all patients complained of oral pain and discomfort. Patients reported increased pain and discomfort when consuming irritating foods. Before treatment, 95.6% complained of a burning sensation and 91.3% of a feeling of tightness. In this group, 82.6% complained of increased salivation. Treatment of control-group patients resulted in complete disappearance of complaints by day 7 (Graph 1).

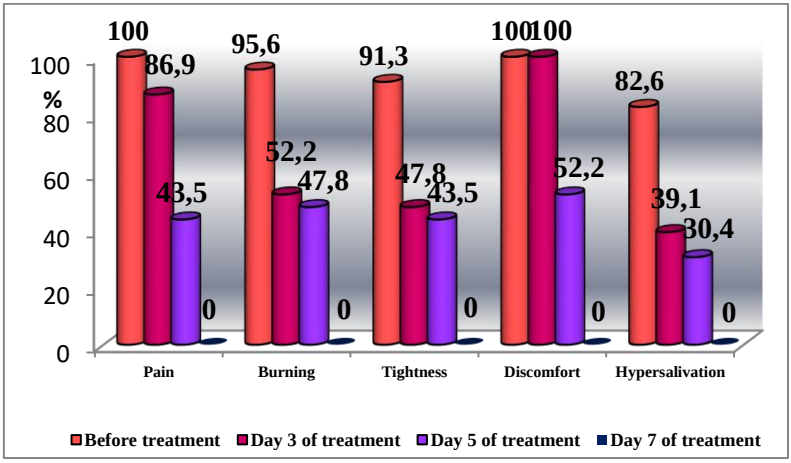


Chart 1. Dynamics of complaints in control-group patients with CRAS and GIT diseases under the influence of treatment.

In the main group, all patients complained of oral pain and discomfort before treatment. A burning sensation in the oral cavity was reported by 93.1% of patients, and 89.6% reported a feeling of tightness. Before treatment, 62.1% complained of increased salivation. All complaints decreased as treatment measures were implemented. On day 5 of treatment, the main pain score was "0". Comprehensive treatment in the main group resulted in complete disappearance of complaints by day 5. The dynamics of complaints in both groups were directly associated with epithelialization of lesions on the oral mucosa. The onset of epithelialization was 3.4 ± 0.1 days in the control group and 2.6 ± 0.1 days in the main group. Complete epithelialization in the main group was recorded at 4.3 ± 0.08 days, while complete epithelialization was observed at an average of 6.4 ± 0.1 days in the comparison group.

Results of dental status assessment. All patients participating in the study underwent comprehensive dental examinations, which made it possible to obtain suitable baseline data for subsequent statistical processing. Dental status was determined using standard indices. In this study, caries intensity was assessed using the DMFT index. The DMFT index provides broad information on the condition of the hard dental tissues and treatment needs. Examination of the hard dental tissues showed a high prevalence of dental caries among patients with chronic recurrent aphthous stomatitis, consistent with the literature (Xabibova N.N., 2019). According to the DMFT index, caries intensity in patients with chronic recurrent aphthous stomatitis was higher than in the control group. Before treatment, mean caries intensity according to the DMFT index was 10.7 ± 0.3, which was 1.7 times higher than in the practically healthy group ($p<0.05$) (practically healthy group: 6.4 ± 0.8). The mean D component was 1.05 ± 0.2, the M component 5.7 ± 0.2, and the F component 3.9 ± 0.2. The study showed that the D component accounted for 9.8% (absolute mean=1.05), the M component for 53.3% (absolute mean=5.7), and the F component for 36.4% (absolute mean=3.9). After comprehensive treatment, the DMFT index, the main index characterizing the condition of hard dental tissues, was reassessed after complete

resolution of oral inflammation, professional hygiene and oral sanitation. The dynamics of qualitative changes affected the DMFT index. Changes in the control and main groups were unidirectional. The DMFT index slightly increased from 11.0 ± 0.5 to 11.6 ± 0.4 in the control group and from 10.4 ± 0.4 to 11.3 ± 0.4 in the main group ($p>0.05$) (Table 2). After treatment, the D component decreased in both the control and main groups, respectively from 1.0 ± 0.3 to 0.21 ± 0.08 and from 1.1 ± 0.2 to 0.2 ± 0.07. At the same time, an increase in the M component was detected after treatment: from 5.8 ± 0.4 to 6.5 ± 0.3 in the control group and from 5.6 ± 0.3 to 6.4 ± 0.3 in the main group. An increase in the F component was also recorded after treatment, from 4.2 ± 0.4 to 4.8 ± 0.4 in the control group and from 3.7 ± 0.3 to 4.6 ± 0.3 in the main group (Table 1).

Table 1.

Main dental indices during treatment of patients with CRAS and gastrointestinal diseases (M ± m)

Dental indices	Practically healthy (n=10)	Control group (n=23)		Main group (n=29)	
		Before treatment	After treatment	Before treatment	After treatment
DMFT	6,4±0,8	11,0±0,5*	11,6±0,4*	10,4±0,4*	11,3±0,4*
D	0,65±0,2	1,0±0,3*	0,21±0,08*^	1,1±0,2*	0,2±0,07*^
M	2,7±0,5	5,8±0,4*	6,5±0,3*	5,6±0,3*	6,4±0,3*
F	3,1±1,2	4,2±0,4	4,8±0,4	3,7±0,3	4,6±0,3^
PMA, %	15,3±3,1	23,4±1,4*	16,5±0,9^	22,9±1,0*	13,8±0,7^
PHP	0,9±0,1	1,7±0,1*	0,9±0,05^	1,8±0,09*	0,93±0,05^

* – statistical significance of differences compared with practically healthy subjects

^ – statistical significance of differences before and after treatment

When periodontal inflammation in patients with Chronic recurrent aphthous stomatitis was assessed using the PMA index (Parma, 1960), the mean value was 23.1 ± 0.8, compared with 15.3 ± 3.1 in the practically healthy group. According to PMA values, patients were divided into the following categories: PMA <30%, corresponding to mild gingivitis, and 30–60%, corresponding to moderate gingivitis. Before treatment, mild gingivitis (PMA up to 30%) was observed in the majority of patients—43 (82.7%)—while a more extensive process was observed in 9 patients (17.3%). Diffuse inflammation and severe gingivitis were not recorded. Before treatment, the mean PHP hygiene index in patients with Chronic recurrent aphthous stomatitis was 1.77 ± 0.07, 1.9 times higher than in the practically healthy group (0.9 ± 0.1; $p<0.05$). Individual analysis showed that unsatisfactory hygiene predominated in 30 patients (57.7%), while satisfactory oral hygiene was observed in 22 patients (42.3%).

Assessment of oral inflammation in patients with Chronic recurrent aphthous stomatitis revealed an increase in the PMA index. Before comprehensive treatment, the mean PMA value was 23.4 ± 1.45% in the control group and 22.9 ± 1.0% in the main group. After comprehensive treatment, this indicator decreased to 16.5 ± 0.9% in the control group and 13.8 ± 0.7% in the main group, and the post-treatment difference between groups was statistically significant ($p<0.05$). The frequency of gingivitis of different severity grades in patients with chronic recurrent aphthous stomatitis during treatment is presented in table 2.

Analysis of the indicators presented in Table 2 shows that patients in both the control and main groups had mild and moderate gingivitis before treatment. After treatment, only mild gingivitis was recorded in both groups.

The presence of inflammatory diseases in acute and chronic stages makes oral care difficult. Poor oral hygiene creates conditions for putrefactive and fermentative processes.

Table 2.
Frequency of gingivitis of different severity grades in patients with CRAS and gastroduodenal ulcer during treatment

PMA index assessment (%)	Control group (n=23)		Main group (n=29)	
	Before treatment	After treatment	Before treatment	After treatment
Mild gingivitis (up to 30%)	17 (73,9%)	23 (100%)	26 (89,6%)	29 (100%)
Moderate gingivitis (30–60%)	6 (26,1%)	-	3 (10,4%)	-

Accumulation of dental plaque and food debris impedes drug penetration and healing of oral mucosal lesions. We investigated and assessed oral hygiene using the PHP hygiene index. The level of oral hygiene according to the PHP index is presented in Table 3. Before treatment, the PHP index was elevated to 1.7 ± 0.1 in the control group and 1.8 ± 0.9 in the main group. After treatment, it decreased to 0.9 ± 0.05 in the control group and to 0.93 ± 0.05 in the main group. As can be seen from the data, oral hygiene was mainly satisfactory after treatment in both groups. In the control group, satisfactory hygiene was observed in 10 patients (43.4%) before treatment and in 18 patients (78.3%) after treatment; 13 patients (56.6%) had unsatisfactory hygiene before treatment. After treatment, good hygiene was identified in 5 patients (21.7%) in the control group.

In the main group before treatment, oral hygiene was satisfactory in 11 patients (37.9%) and unsatisfactory in 18 patients (62.1%). After comprehensive treatment, hygiene improved to a satisfactory level in 23 patients (79.3%), while good hygiene was achieved in 6 patients (20.7%).

No unsatisfactory hygiene values were recorded after treatment. Thus, comprehensive treatment in both groups produced positive changes in oral hygiene, although the persistence of predominantly

satisfactory rather than good hygiene indicated the need to include local hygiene measures in the treatment complex.

Table 3.

Oral hygiene level according to the PHP index in patients with CRAS and gastroduodenal ulcer during treatment

PHP index assessment	Control group (n=23)		Main group (n=29)	
	Before treatment	After treatment	Before treatment	After treatment
Good (0.1–0.6)	-	5 (21,7%)	-	6 (20,7%)
Satisfactory (0.7–1.6)	10 (43,4 %)	18 (78,3%)	11 (37,9%)	23 (79,3%)
Unsatisfactory (>1.7)	13 (56,6%)	-	18 (62,1%)	-

Results of cytomorphological studies. Cytomorphological investigations of the oral cavity are scientific medical studies based on microscopic examination of cellular samples obtained from the oral mucosa. These studies help identify normal cellular structure and pathological changes in the oral cavity. Cellular composition was investigated using scrapings from the oral mucosa. In patients with chronic recurrent aphthous stomatitis, changes in the cytological profile are manifested by increased numbers of neutrophils, lymphocytes and monocytes and a decreased number of epithelial cells. Neutrophilia is accompanied by reduced functional phagocytic activity and an increased percentage of destructive neutrophil forms in the FAN-2 test. The cytological method makes it possible to assess the hygienic condition of the oral cavity. The composition of cellular elements of the oral mucosa has important diagnostic value in determining the tactics of therapeutic and preventive measures in chronic recurrent aphthous stomatitis.

The changes identified in the cytomorphological picture of the oral mucosa highlighted the importance of assessing local immunity

after treatment by different methods and demonstrated a positive effect on non-specific immunity of the oral mucosa. In this regard, it was particularly important to evaluate the direction of changes in cellular parameters of the oral mucosa during treatment. The results of cytomorphological studies obtained before and after treatment in the patient groups are presented in table 4.

Elements of the inflammatory cell series—neutrophils, lymphocytes and monocytes—were detected in smears from the oral mucosa. Erythrocytes were present in small or larger amounts. Bacteria were consistently present, including cocci, bacilli and fungi of the genus Candida. Cytomorphological studies were performed in 23 patients in Group 1 and 29 patients in Group 2. Cytograms in both groups were studied before and after treatment. In Group 1, a sorbent was used for local application, whereas comprehensive treatment in Group 2 also included antioxidant. As shown by the data in Table 4, the numbers of lymphocytes and neutrophils were increased in patients with stomatitis. Monocytes (macrophages) were also increased; before treatment, the mean level was $9.9 \pm 0.4\%$ in Group 1 and $9.5 \pm 0.2\%$ in Group 2, approximately 1.5 times higher than in practically healthy subjects ($p<0.05$). Redistribution of cellular composition was manifested, on the one hand, by increases in lymphocytes, neutrophils and monocytes and, on the other hand, by decreases in epithelial cells to $14.0 \pm 1.2\%$ and $15.4 \pm 1.1\%$, respectively ($p<0.05$). FAN-1, an indicator characterizing neutrophil functional activity, decreased to $6.2 \pm 0.3\%$ in Group 1 and $6.0 \pm 0.3\%$ in Group 2. Reduced functional activity of neutrophils in the FAN-1 reaction indicates a decrease in the percentage of neutrophils participating in phagocytosis of the resident oral flora. The FAN-2 value averaged $9.0 \pm 0.5\%$ in Group 1 and $9.8 \pm 0.3\%$ in Group 2 and was statistically 1.9–2.2 times higher than in practically healthy subjects ($p<0.05$). The increased FAN-2 test indicated a higher percentage of destructive neutrophils in patients with stomatitis before treatment. After treatment using a sorbent and antioxidant, patients in both groups showed clinical improvement, which was consistent with cytomorphological findings. In both groups, treatment resulted in a significant decrease in neutrophils, a

reduction in destructive forms and an increase in the percentage of phagocytic cells. After treatment, the proportion of neutrophils decreased by 25.3% in Group 1 and 34.8% in Group 2. Monocytes decreased by 17.2% in Group 1 and 31.6% in Group 2. Lymphocytes decreased more markedly in Group 2 (22.9%) and by 14% in Group 1.

The number of phagocytes in the FAN-1 reaction increased by 15.1% in Group 1 and more substantially, by 31%, in Group 2 receiving topical sorbent and antioxidant vitamin E. In the FAN-2 test, degeneratively altered phagocytes decreased by 20% in Group 1 and 50% in Group 2. These cytomorphological findings indicate a reduction of the inflammatory process in the oral mucosa and increased non-specific resistance of the oral cavity in patients with stomatitis and gastrointestinal tract diseases. More pronounced positive cytomorphological dynamics were observed in Group 2, supporting the appropriateness of comprehensive treatment with a sorbent and antioxidant (table 4).

Table 4.
Results of cytological studies in patients with CRAS during treatment (M ± m)

Indicators	Practically healthy (n=10)	Group 1 (n=23)		Group 2 (n=29)	
		Before treatment	After treatment	Before treatment	After treatment
Neutrophils, %	22,7±0,5	38,7±0,5	28,9±0,3	37,6±0,7	24,5±0,4
Monocytes, %	6,3±0,4	9,9±0,4	8,2±0,2	9,5±0,2	6,5±0,2
Lymphocytes, %	15±0,5	21,1±0,5	19,0±0,4	21,4±0,3	16,5±0,3
Epithelial cells, %	41,7±1,1	14,0±1,2	29,2±0,7	15,4±1,1	39,2±0,5
FAN– 1, %	9,9±0,6	6,2±0,3	7,3±0,1	6,0±0,3	8,7±0,1
FAN– 2, %	4,4±0,4	9,0±0,5	7,2±0,3	9,8±0,3	4,9±0,2

Results of biochemical studies. In patients with chronic recurrent aphthous stomatitis, changes in the protein component of oral fluid were also manifested by a decrease in globulins to 1.1 ± 0.03 g/L and in the albumin/globulin (A/G) ratio to 0.94 ± 0.04. The globulin level was 15.4% lower than in practically healthy subjects ($p<0.5$), whereas the A/G ratio was 7% lower ($p>0.05$). Before treatment, mean albumin level in patients with stomatitis was 0.99 ± 0.03 g/L, which was 1.3 times lower than in practically healthy subjects ($p<0.05$).

During exacerbation of the disease, total protein decreased 1.2-fold, albumin 1.3-fold and globulins 1.2-fold. Strong positive correlations were established between total protein and albumin levels ($r=0.6$) and between total protein and globulin levels ($r=0.5$), reflecting the presence of clinical manifestations in the oral cavity.

The following metabolic enzymes were determined in oral fluid: alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and aminotransferases (ALT and AST). Examination of oral fluid in patients with chronic recurrent aphthous stomatitis also revealed a significant increase in ALT and AST activity, allowing assessment of the severity of the inflammatory process in the oral cavity, because during inflammation proteins undergo proteolysis, increasing the amount of free amino acids and simultaneously increasing enzyme activity. Thus, the activity of metabolic enzymes involved in regulation of oral homeostasis is increased in patients with chronic recurrent aphthous stomatitis.

The activity of the antioxidant system in oral fluid was assessed by the levels of the secondary nitrogen-containing antioxidants urea and uric acid, as well as another antioxidant, total bilirubin. The study revealed decreased levels of secondary non-enzymatic nitrogen-containing antioxidants—urea and uric acid. In patients with CRAS, urea content in oral fluid was reduced and averaged 7.4 ± 0.07 mmol/L. Another biochemical indicator, uric acid in oral fluid, was also reduced 1.25-fold compared with practically healthy individuals ($p<0.05$). Assessment of bilirubin in oral fluid showed a decrease associated with the inflammatory

process of the oral mucosa. Mean bilirubin level was 1.5 ± 0.06 μmol/L, 2.3 times lower than in practically healthy subjects. In patients with CRAS and gastrointestinal tract diseases, bilirubin decreased by 57.1%, the nitrogen-containing antioxidant urea by 12.9%, and uric acid by 20%. On the basis of these findings, reduced antioxidant defense of the oral cavity can be stated in patients with chronic recurrent aphthous stomatitis and gastrointestinal tract diseases.

Thus, laboratory findings indicate that comprehensive treatment aimed at preventing exacerbation of chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer can provide effective results. Changes in biochemical parameters of oral fluid during treatment were analyzed in patients with chronic recurrent aphthous stomatitis. Before treatment, the levels of total protein, albumin and globulins were reduced in both groups. Treatment affected biochemical parameters of oral fluid, with the degree of change depending on the therapeutic method. Comparative analysis of albumin levels during treatment showed a statistically significant increase in Group 2. Against the background of comprehensive antioxidant therapy in Group 2, albumin increased from 0.94 ± 0.04 g/L to 1.32 ± 0.01 g/L ($p<0.05$), whereas the increase in Group 1 was not significant. Total protein increased in both groups, but the increase in Group 2 was statistically significant compared with pretreatment data ($p<0.05$). Treatment also affected globulin levels in oral fluid. During treatment, globulins increased from 1.1 ± 0.05 g/L to 1.25 ± 0.03 g/L in Group 1 and from 1.1 ± 0.05 to 1.14 ± 0.03 g/L in Group 2. As a result of changes in albumin and globulins, the A/G ratio was 0.93 ± 0.04 in Group 1 and 1.18 ± 0.05 in Group 2. Thus, when comparing the treatment methods in terms of the protein component of oral fluid, better study outcomes in Group 2 of patients with CRAS against a background of gastrointestinal tract diseases may be explained by the use of antioxidants in treatment (Graph 2).

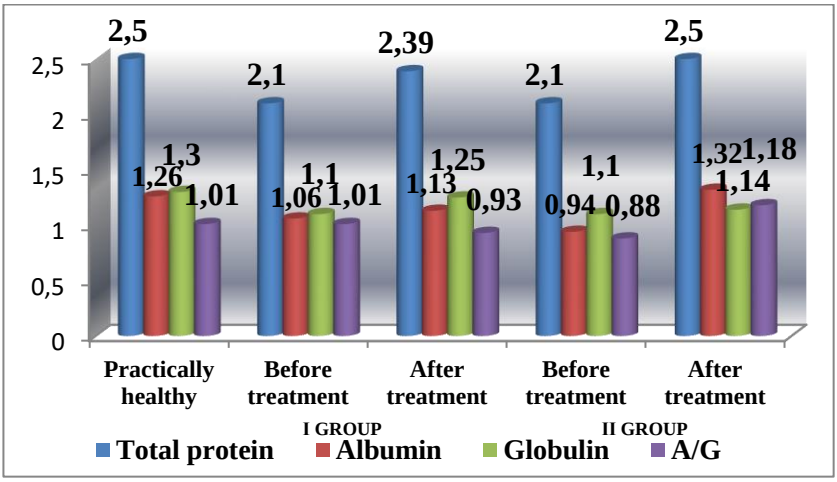


Chart 2. Dynamics of oral-fluid protein content in patients with CRAS during treatment against the background of GIT disease.

An important indicator of the inflammatory process is increased intensity of free-radical oxidation and reduced antioxidant protection. According to the study results, levels of secondary antioxidants in oral fluid were decreased before treatment in patients with CRAS. Reduced antioxidant defense in the oral cavity may contribute to further progression of CRAS. A decrease in antioxidant protection promotes activation of free-radical oxidation and accumulation of lipid peroxidation (LPO) products in the oral cavity. LPO products may damage major connective-tissue components such as collagen. The multistage antioxidant system consists of enzymes and low-molecular-weight substances, as well as components such as urea and uric acid. Considering the complex pathogenesis of chronic recurrent aphthous stomatitis, a rigorous analysis of biochemical parameters should include evaluation of antioxidant levels. Because antioxidant activity was reduced in patients in the main group, the antioxidant Alligat was included in the comprehensive treatment.

Graph 3 presents the results of determination of secondary antioxidants in oral fluid during treatment. In the main group, in addition to conventional therapy, the sorbent Enterosgel and the

antioxidant Alligat were included in comprehensive treatment. The data show that after treatment the urea level increased in the main group to an average of 8.3 ± 0.06 mmol/L, compared with 7.8 ± 0.07 mmol/L in the control group, which was 6% higher ($p<0.05$). Antioxidant administration in the main group also increased uric acid, another secondary antioxidant. After treatment, uric acid in oral fluid was 157.6 ± 1.5 μmol/L in the main group and 148.2 ± 1.9 μmol/L in the control group, 5.9% higher in the main group ($p<0.05$). The study results also show that bilirubin increased significantly in the main group (3.7 ± 0.1 μmol/L versus 2.7 ± 0.08 μmol/L, $p<0.05$).

In patients with chronic recurrent aphthous stomatitis against the background of gastric and duodenal ulcer, the level of antioxidant defense in the oral cavity is reduced. The use of sorbents and antioxidants increases antioxidant potential in terms of secondary antioxidants.

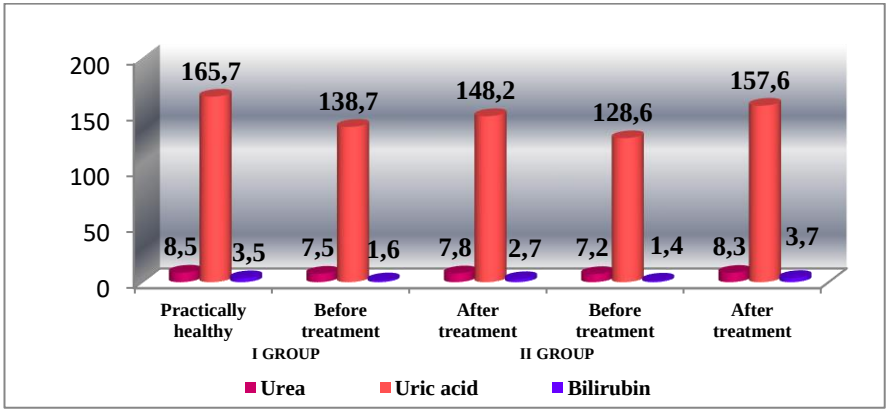


Chart 3. Dynamics of changes in the level of secondary antioxidants in oral fluid in patients with CRAS and GIT disease.

Inclusion of the antioxidant preparation "Alligat" in comprehensive therapy makes it possible to enhance antiradical protection of the oral cavity. Before treatment, the activity of the studied enzymes was increased in patients with CRAS in both the control and main groups. Analysis of alkaline phosphatase activity in oral fluid after treatment showed a statistically significant difference

in this enzyme between the control and main groups ($p<0.001$). The percentage difference before and after treatment was 24.2% in the control group and 41% in the main group.

Along with changes in alkaline phosphatase, LDH activity also differed in patients with chronic recurrent aphthous stomatitis. After treatment, LDH activity decreased in both groups. LDH activity in oral fluid decreased by 65.6% in the control group and by 77.1% in the main group. Treatment in the control group, however, did not fully normalize the activity of metabolic enzymes in oral fluid. After treatment in control-group patients with chronic recurrent aphthous stomatitis, levels of alkaline phosphatase (28.3%), LDH (37.3%), ALT (33.8%) and AST (27.7%) remained different from those of practically healthy subjects. The post-treatment data in the control group indicate that conventional therapy does not significantly affect metabolic enzyme activity (Graph 4).

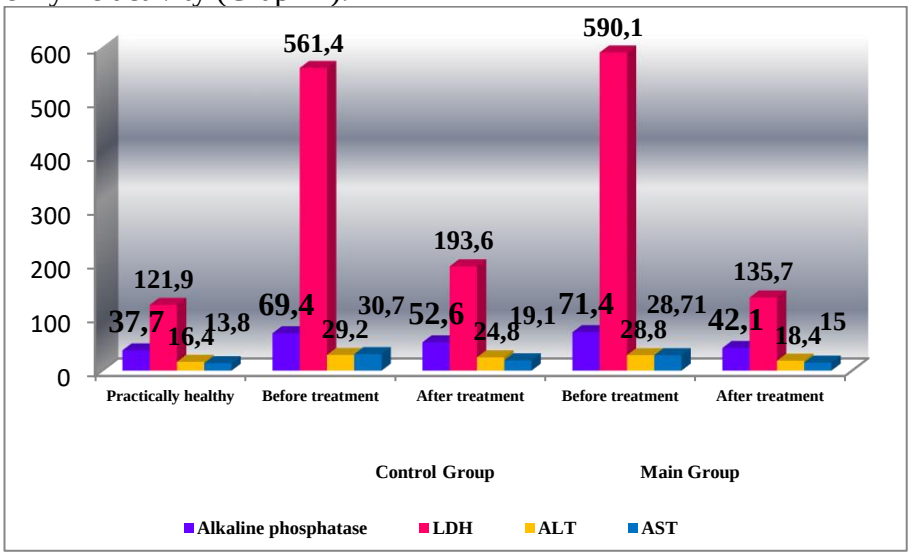


Chart 4. Dynamics of enzyme activity in oral fluid

The drugs used as basic therapy according to the protocol for treatment of patients with chronic recurrent aphthous stomatitis significantly improve the patients' condition; however, the

persistently elevated levels of metabolic enzymes in oral fluid indicate incomplete normalization. Therefore, the existing treatment regimen needs to be supplemented to improve treatment effectiveness in CRAS. In modern medical science, widespread use of vitamins with antioxidant effects for prevention and treatment of many diseases remains relevant. The obtained data indicate that vitamins with antioxidant effects should be added to the existing basic treatment of patients with CRAS. Another criterion of treatment effectiveness is the duration of remission. The longest recurrence-free period was recorded in the main group and was 148 days, whereas in the control group it was shorter, at 122 days. Patients in the main group received local treatment with a sorbent and an antioxidant, demonstrating the effectiveness and prolonged action of this treatment method.

The study results show that during treatment of patients with chronic recurrent aphthous stomatitis, immunological protection of the oral mucosa was restored both with conventional therapy and with therapy combining antioxidants and a sorbent. After treatment, there was a significant decrease in neutrophils, a reduction in destructive forms and an increase in the percentage of phagocytic cells. After basic therapy, neutrophils decreased by 25.3%, monocytes by 17.2% and lymphocytes by 14%. After comprehensive therapy, a more pronounced decrease in immune cells was recorded (neutrophils 34.8%, monocytes 31.6%, lymphocytes 22.9%). Thus, positive dynamics were observed predominantly in the group receiving comprehensive therapy, supporting the appropriateness of using antioxidants and sorbents in patients with chronic recurrent aphthous stomatitis. Based on data on the condition of the oral mucosa and dental status in patients with gastrointestinal diseases, as well as dynamic assessment of non-specific oral resistance and biochemical parameters of oral fluid, it can be concluded that the most effective comprehensive therapy for chronic recurrent aphthous stomatitis includes drugs with antioxidant properties and sorbents in the local treatment regimen.

CONCLUSIONS

1. Changes in the oral mucosa were found to be widespread in patients with gastrointestinal pathologies. The most common clinical signs were dryness of the mucosa and tongue coating (100%), edema (62.5%), pain syndrome (39.6%), aphthous lesions (39.7%) and hyperemia (37.4%). The severity of changes in dental status was associated with the clinical course of chronic recurrent aphthous stomatitis [8,9,11,12,20].
2. The frequency of different severity grades of chronic recurrent aphthous stomatitis was determined in the examined patients with gastric and duodenal ulcer. Mild chronic recurrent aphthous stomatitis predominated (61.5%), while the moderate form was observed less frequently [7,13].
3. Biochemical and immunological changes in the oral cavity were identified in different severity grades of chronic recurrent aphthous stomatitis. Increased activity of metabolic enzymes (alkaline phosphatase, lactate dehydrogenase) was more pronounced in moderate disease. At this severity, neutrophil phagocytic activity decreased by 7.9%, the level of destructive neutrophils increased by 9%, and total protein, albumin and globulin levels in oral fluid decreased 1.3-fold ($p<0.05$) [14,18,19,25,31].
4. The clinical effectiveness of comprehensive treatment based on the combined use of a sorbent and an antioxidant was established. Treatment accelerated epithelialization of aphthae 1.5-fold and prolonged remission 1.2-fold compared with conventional treatment [6,15,21,26,27].
5. Comprehensive treatment had a positive effect on antioxidant and enzymatic activity in oral fluid and on indicators of non-specific oral immunity. Secondary antioxidant levels increased by 31.2%, compared with a 17% increase during conventional treatment, while the alkaline phosphatase value decreased by 41%. Among immunological indicators, neutrophils decreased

by 15.2%, monocytes by 20.7% and lymphocytes by 13.2% ($p<0.05$) [22,24,28].

PRACTICAL RECOMMENDATIONS

1. Clinical examination and treatment of patients with recurrent aphthous stomatitis associated with gastrointestinal pathologies should be carried out collaboratively by a dentist and a gastroenterologist.
2. To improve the effectiveness of comprehensive treatment of recurrent aphthous stomatitis in patients with gastric and duodenal ulcers, professional oral hygiene and oral sanitation should be performed. This includes the removal of dental plaque and calculus, treatment of carious teeth and elimination of other sources of infection, as well as identification and correction of local traumatic factors that may damage the oral mucosa. Patients should be instructed in proper individual oral hygiene practices and advised to undergo regular dental check-ups.
3. To improve treatment effectiveness in patients with chronic recurrent aphthous stomatitis who have gastric and duodenal ulcer and reduced antioxidant defense of the oral cavity, the sorbent “Enterosgel” should be used topically on aphthae 3 times daily until complete epithelialization of the aphthous lesions, together with the antioxidant “Alligat” (per os), 1 capsule once daily.

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