WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

EFFICIENCY OF TREATMENT FOR RECURRENT AFTHOUS STOMATITIS OF THE OROPHARYNGIAL REGION IN PATIENTS WITH CHRONIC CHOLECYSTITIS

Kamilov Haydar Pozilovich
Head of the Department, Doctor of Medical Sciences, Professor
Department of Hospital Therapeutic Dentistry TGSI
Tashkent State Dental Institute, Uzbekistan

Ibragimova Malika Khudayberganovna
Doctor of Medical Sciences, Associate Professor of the Department
Department of Hospital Therapeutic Dentistry TGSI
Tashkent State Dental Institute, Uzbekistan

Ubaydullaeva Nigora Ilyasovna
Assistant of the Department
Department of Hospital Therapeutic Dentistry TGSI
Tashkent State Dental Institute, Uzbekistan

Abstract

Chronic recurrent aphthous stomatitis (CRAS) is a chronic inflammatory disease of the oral mucosa and characterized by the appearance of aphthous ulcers with a long course and periodic remissions and exacerbations. Much attention is paid to somatic diseases, which aggravate the course of CRAS. V.A. Epishev observed chronic recurrent aphthous stomatitis in gastrointestinal diseases in 15.2% of cases, according to G.V. Banchenko - 12%.

The factors provoking relapses include microorganisms that in the process of vital activity, especially during death, release bacterial endotoxins, which have both antigenic and toxic features. An increased process of tissue alteration during the activation of catabolic processes is one of the causes of endogenous intoxication (Sidelnikova V.I., Chernitskiy A.E., Retsky M.I., 2015). In chronic cholecystitis, CRAS is often observed in the oropharyngeal region. The drug Baktizidime was introduced as the treatment regimen of CRAS of the oropharyngial region of the main group and the drug Eludril into the comparison group.

Keywords: CRAS, oropharyngeal region, aphthae, ulcers, chronic cholecystitis, Baktizidim.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Relevance

Chronic recurrent aphthous stomatitis (CRAS) is a chronic inflammatory disease of the oral mucosa and characterized by the appearance of aphthous ulcers with a long course and periodic remissions and exacerbations. Much attention is paid to somatic diseases, besides that psychological stress, anxiety and depression that aggravate the course of CRAS were assessed in patients with recurrent aphthous stomatitis and compared with normal patients. [1, 6, 8, 13, 15]. V.A. Epishev observed chronic recurrent aphthous stomatitis in 15.2% of cases [4] and according to G.V. Banchenko – only in 12% cases [2].

According to modern concepts, the leading agent determining the commonality of the adaptation mechanism and pathology in inflammation is intestinal endotoxin, which is formed during the death of gram-negative intestinal microflora, namely, Escherichia coli. It is known that when microorganisms die, they release bacterial endotoxins that have both antigenic and toxic properties. The increased process of tissue alteration during the activation of catabolic processes is one of the causes of endogenous intoxication.[3,5,7,9,10,11,12,14].

A 36-year-old woman had refractory ankylosing spondylitis. In 2010, she had ulcerations of the oral cavity during the treatment of the main disease, in 2016, due to an exacerbation of intestinal ileo-pancolitis, aphthous lesions of the oral mucosa appeared again. After corticosteroid therapy, the aphthae had a favorable course, suggesting an immunological factor between the two episodes[15].

The location of aphthaes in CRAS, according to different authors, occurs on the buccal mucosa (45.6%), transitional folds (45%), the tip and lateral surface of the tongue (6.1% -14%), the sublingual region (4% - 7%), upper and lower lips (41.2%), soft palate (2%) [5,6,11].

However, sometimes patients are treated with chronic recurrent aphthaes located in the posterior part of the oral cavity, palatine arch, posterior parts of the soft palate, i.e. oropharyngeal region, near the uvula. The unusual location of the aphthae is combined with the unusual shape of the aphthae. Clinically, aphthae are large and on average from 1.8-2.0 mm or more, irregular shape, very painful, covered with a white or grey coating and does not heal for a long period. In the structure of general somatic pathology of patients with CRAS from 37 people with gastrointestinal tract pathology (100%), 17 (45.9%) had chronic cholecystitis, S.Yu. Kosyuga et al., (2015). Moreover, aphthous stomatitis in the background of this group of patients develops of not so much a single, but as a combined gastroduodenal pathology [9].

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Purpose of the Study

Improving the treatment of chronic recurrent aphthous stomatitis in patients with chronic cholecystitis using the drug Baktizidim.

MATERIAL AND METHODS

The material for the analysis and conclusions were the data of examination of 96 patients who clinically had one systemic pathology. Amongst all of the examined patients, 54 (main group) had chronic recurrent aphthous stomatitis (CRAS) of the oropharyngeal region combined with chronic cholecystitis, 42 (comparison group) had chronic recurrent aphthous stomatitis (CRAS) of the oropharyngeal region combined with chronic cholecystitis. As indicators of the norm, we used the results of a survey of 20 healthy individuals of comparable gender and age, which are controls. Clinical and biochemical studies were carried out. Clinical examination of patients began with clarification of complaints and collection of anamnesis. The oral mucosa was assessed by the presence of lesion elements, their number, localization, severity of inflammation, and their size. The examination of the oral cavity was carried out on the recommendation of the WHO. Biochemical studies included determination of average mass molecules (AMM), reflecting the presence of unidentified substances of various chemical nature and characterized by a molecular weight of 300 to 5000 D. Indicators of endogenous intoxication and protective systems of the oral fluid are presented in table no.2.

Oral fluid and blood were used as material for biochemical research. The oral fluid was taken in the morning on an empty stomach; the patient must first rinse the oral cavity with saline. Blood was taken from all patients in the morning on an empty stomach by puncture of the ulnar vein with a needle, from which plasma was subsequently obtained.

The level of AMM was investigated by the method of N.I. Gabrielyan [3] in the ultraviolet range in the continuous scanning mode at wavelengths from 220 to 300 nm. The level of the average molecular pool for plasma was assessed by optical density. In the spectrophotometric determination of SMP_{260} and SPM_{280} [40], the optical density of the samples against water was studied in the ultraviolet range, at λ 260 nm (SMP_{254}) and λ 280 (SMP_{280}). The number of SMPs was calculated using the Kalkar method: $SPM_{254} = (E \cdot 0.74) \cdot 10$, and $SPM_{280} = (E \cdot 1, 45) \cdot 10$ and expressed in g/l 1.45 and 0.74 - the calculated Kalkar coefficients that translate plasma volume(PV)/ ml with SI system - g/l. Indicators of endogenous intoxication and protective systems of the oral fluid are presented in table no.2.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

OBTAINED RESULTS AND DISCUSSION

We examined the patients with CRAS of the oropharyngeal region with an underlying disease of chronic cholecystitis. 96 patients were examined. The distribution of patients is shown in Table no.1.

Table no.1 Distribution of patients with CRAS in chronic cholecystitis by gender and age

Gender		Patients' age, years					Total
		21-30	31-40	41-50	51-60	61-70	
Women	abs	9	11	15	14	2	51
	%	17.6	21.5	29.4	27.4	3.9	53.1
Men	abs	10	9	12	11	3	45
	%	22.2	20.0	26.7	24.4	6,7	46.8
Total	abs	19	20	27	25	5	96
	%	19.8	20.8	28.1	26.0	5.2	100.0

It can be seen from Table no.1, out of the total number of patients (96) CRAS in women were observed 51 (53.5%), slightly more than men - 45 (46.8%). In terms of age, CRAS was observed in patients aged from 21 to 70 years. There were 51 women (53.7%) and 45 men (46.8%). The patients were divided into two groups: main and comparison. 20 healthy people served as control group.

The treatment methods of the main group and the comparison group is consisted of local application of anesthesia with 2% lidocaine solution, 0.05% chlorhexidine solution for antiseptic treatment, enzymatic treatment with trypsin, Baktizidim drug - in the main group and Eludril - in the comparison group.

In general treatment in both groups were used: Desensitizing drug (Sodium thiosulfate 30% -10.0 ml 5-7 days intravenously); Antihistamine (Zaditen 1 mg, twice a day, 10-14 days); Detoxification drug (Rheosorbilact 200 ml intravenous drip, then jet stream for 3-5 days); Probiotic (Enterogermina suspension inside 1 billion 1 time i / d); Hepatoprotector (Ursosan10-15 mg / kg at night for 1-2 months); Regeneration stimulator (Solcoseryl 5.0 + 100.0 physical solution intravenous); Vitamin C 250 mg 3 times a day and calcium carbonate powder 1 teaspoon a day. The course of treatment is 6-8 weeks.

According to the severity, the patients of both the main group (54) and the comparison group (42) were divided into the mild, moderate-severe and severe forms of CRAS.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Biochemical Research

Excessive intake of endotoxin is possible with pathology of the intestine, liver, activation of the sympathoadrenal system. An overload of the systems and organs of endotoxin elimination causes secondary immune deficiency, which, in turn, causes acute and chronic inflammatory processes of various localization. In this regard, we determined the indices of endogenous intoxication of the oral fluid in patients with CRAS of the oropharyngeal region with chronic cholecystitis before (table no.2) and after treatment.

Table no. 2 Indicators of endogenous intoxication of the oral fluid in patients with CRAS of the oropharyngeal region with chronic cholecystitis before treatment

The studied indicators	Healthy patients n = 20	Patients with CRAS with chronic cholecystitis(women) n = 54	Patients with CRAS with chronic cholecystitis(men) n = 42
Average mass molecules E_{254} (conventional units)	0.213 ± 0.001	0.381 ± 0.05 *	0.393 ± 0.018 *
Average mass molecules E_{280} (conventional units)	0.311 ± 0.001	0.491 ± 0.003 *	0.419 ± 0.015 *
IL - 8 (pg / ml)	2.68 ± 0.30	22.9 ± 1.64 *	22.8 ± 1.63 *
Content of polymorphonuclear neutrophils (%)	56.5 ± 2.17	77.8 ± 1.12 *	76.7 ± 1.35 *

Reliability of differences P≤0.05 when compared with healthy patients

Analysis of the results of the study presented in table 2. showed that the content of AMM (E_{254}) in patients with CRAS of the oropharyngeal region with chronic cholecystitis was significantly increased and was equal to 0.381 + 0.005 conventional units (with a norm of 0.213 + 0.011 conventional units), which is 1.7 times higher than the initial values. In patients with CRAS of the oropharyngial region with chronic cholecystitis in the comparison group, the AMM index (E_{254}) was 0.393 ± 0.018 conventional units, which is 1.8 times higher than the initial values. The results of the study of endogenous intoxication in patients with CRAS with somatic pathology indicate the accumulation of intermediate products of intensive proteolysis with a molecular weight of 1000-2000 daltons, as well as other organic compounds (Table no.2).

In contrast to the state of the indicators of AMM (E_{254}) studied at a wavelength of 254 nm, the level of AMM (E_{280}) determined at a wavelength of 280 nm was also increased in the examined patients. So, if the level of AMM (E280) with wavelength in healthy people averaged 0.311 ± 0.001 conventional units, then in patients with CRAS of the oropharyngeal region with chronic cholecystitis of the main group, this indicator was 0.491 ± 0.003 conventional units, which is 1.6 times exceeded the original values. In the comparison group of the group of patients with CRAS of the oropharyngial region with chronic cholecystitis, this indicator was 0.419 ± 0.015 conventional units, which was 1.3 times higher than the initial indicators. The increase in AMM (E_{280}) detected at wavelength in patients with CRAS of the main group, in our opinion, is due to the accumulation of biologically active substances in the blood with a molecular weight of 200 to 500 daltons,

In the examined patients, the distribution coefficient equal to the ratio AMM_{280} / AMM_{254} in patients with CRAS in the main group was reduced by 1.3 times, which indicates the failure of the filtration capacity of the kidneys, since normally up to 95% of AMM is removed by glomerular filtration (O. V. Yudakov, 2006).

As for proinflammatory cytokines (IL-8), it can be seen from the presented results of the study that the level of cytokine IL-8 in saliva of the examined patients of the CRAS of the main group exceeded the initial level by more than 8 times and amounted to 22.9 ± 1.64 pg/ml (in normal conditions 2.68 ± 0.30 pg/ml). Apparently, high levels of IL-8 in mixed saliva are aimed at attracting neutrophils to the area of inflammation, where these cells are involved in the sanitation of the area of necrosis, and then in the remodeling of newly formed tissues (N.A. Zorin, 2009) (table no.2).

For patients with CRAS of the main group, an increase in the percentage of polymorphonuclear neutrophils (PMNN) is also relevant (PMNN in healthy people was 56.5 ± 2.17%) to values of 77.8 + 1.12%. In patients with CRAS of the comparison group, the level of PMNN was 76.7 ± 1.35%, which exceeded the initial level by 1.4 times ($P < 0.05$) in both study groups. Probably, it is connected with the high levels of neutrophils in the blood revealed by us in the examined patients of the main and the comparison group with CRAS of the oropharyngeal region with chronic cholecystitis.

Thus, the analysis of the results obtained from patients with CRAS of the oropharyngeal region with chronic cholecystitis in the studied groups indicates the increase of endogenous intoxication, which is accompanied by an increased synthesis of neutrophils involved in the inflammatory process, which enhances the process of cell apoptosis and tissue regeneration in the inflammation area.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Clinical examination of CRAS of the oropharyngial region in patients with chronic cholecystitis (main group and comparison groups) was carried out.

Table no.3 The condition of oral mucosa in patients with CRAS before treatment

The condition of oral mucosa	Main group, n = 54		Comparison group, n = 42		χ2	P
	abs.	%	abs	%		
Pain	39	72.2	31	73.8	0.03	0.854
Burning	35	65.3	27	64.3	0.01	0.915
Discomfort	40	73.6	29	69.0	0.27	0.601
Smell from the mouth	23	43.1	19	45.2	0.05	0.821
Dry mouth	43	77.8	27	66.7	1.69	0.194
Disturbance of the general condition of the body	37	68.1	25	61.9	0.45	0.504
Regional lymph nodes	17	30.6	14	33.3	0.09	0.758
Hyperemia	36	66.7	29	66.7	0.00	1,000
Edema	21	38.9	15	35,7	0.11	0.736
Pronounced depth of aphtaes	27	50.0	20	47.6	0.06	0.806

As can be seen from Table no.3, a clinical examination of patients with CRAS of the oropharyngeal region with chronic cholecystitis of the main group showed that pain observed in 39 patients(72.2%) and in 31 patients (73.8%) in comparison group; burning observed in 35 patients(65.3%) and in 27 patients (64.3%) of comparison group patients. In the main group discomfort, bad breath and dry mouth were observed accordingly in 40 (73.6%); 23 (43.1%) and 43 (77.8%) patients with CRAS; and respectively in 29 (69%); 19 (45.2%) and 27 (66.7%) patients with CRAS from comparison group. Violation of the general condition and an increase in regional lymph nodes are noted, respectively, in 37 (68.1%), 17 (30.6%) patients with CRAS of the main group; in 25 (61.9%), 14 (33.3%) - in patients with CRAS in the comparison group. Hyperemia, edema and a pronounced depth of aft are observed, respectively, in patients with CRAS in the main group, observed in 36 (66.7%); 21 (38.9%); 27 (50%) and 29 (66.7%); 15 (35.7%); at 20 (47,)

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Clinical results of examination of patients with CRAS of the oropharyngeal region in patients with chronic cholecystitis in the main and comparison group

Patients with CRAS of the main group with a mild form with chronic cholecystitis complained of the presence of single aphthae in the oropharyngeal region. The general condition was not disturbed, however, complaints were of pain and burning during meals. On examination, there are 1-3 aphthae, with a hyperemic rim around and a slight edema, the surface of the aphth is covered with a thin fibrinous coating. The diameter of these aphthae ranges from 0.8 to 1.2 mm.

The number of relapses in these patients is observed 1-2 times a year, the duration of relapses is from 7-10 days, the duration of remission is 6-7 months.

Patients with an average degree of CRAS in the oropharyngeal region with chronic cholecystitis mainly complained of a violation of the general condition of the body, which was expressed in moderate headaches. Frequent erosion of the aphthae is observed, according to the patients, sometimes ulcers appeared at the site of the aphthae, covered with a gray-white coating. The number of aphthae is not more than 4-6, however, the diameter increased and was in the range of 1.3-1.7 mm. An inflammatory infiltrate, hyperemia and edema are observed while analyzing the state of erosion of the edges. The number of relapses in these patients was 2-3 times a year, the duration of relapses was 10-13 days, the duration of remission was 4-6 months.

In patients of the main group with a severe course of CRAS, there was significant hyperemia and edema with inflammatory infiltrate within the lesion elements - aphthae and erosions covered with fibro-necrotic plaque, regional lymph nodes are enlarged and painful, the diameter of these aphthae ranged from 1.8-2.0 mm. The number of relapses in severe CRAS was 4-5 times a year, the duration of remission was 2-3 months.

The duration of the disease of mild CRAS in the main group was up to 1 year in 4 (22.2%) patients, 5 (27.7%) people had a history of disease duration of 3-5 years, 6 (33.3%) people had the duration of the disease 5-10 years, in 3 (16.6%) people, CRAS was observed more than 10 years ago. We did not observe patients with a moderate and severe form of CRAS in the main group with a history of disease duration up to 1 year. 8 (44.4%) patients of the main group had a disease duration of 3-5 years. 6 (33.3%) patients suffered from CRAS for 5-10 years, 4 (22.2%) patients had a history of the disease for more than 10 years.

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

In the main group, 2 patients with severe CRAS (11.1%) had a disease duration of 3-5 years, 8 (44.4%) patients had a disease duration of 5-10 years, more than 10 years had a disease duration of 8 (44, 4%) of CRAS patients. The baseline incidence of mild relapses in the study group was 1.29 versus 1.38 in the comparison group; in the moderate-severe form of the main group - 2.25 versus 1.71 in the comparison group; In severe form of CRAS, the recurrence rate is 2.73 in the main group versus 2.6 in the comparison group.

Dynamics of the assessment of endogenous intoxication of the oral fluid in patients with CRAS of the oropharyngeal region after treatment

As can be seen from the presented research results (table no.4) in the main group in patients with CRAS of the oropharyngial region with chronic cholecystitis with complex therapy with the inclusion of the drug Baktizidime, a significant decrease in endogenous intoxication of AMM was noted by 35% E_{254} and E_{280} - by 44% (P <0.05) in relation to the indicators before treatment, when compared with the group of healthy individuals, the decrease is 1.6 times and 1.4 times, respectively. During the traditional treatment of CRAS of the oropharyngeal region with chronic cholecystitis in the comparison group, the level of AMM decreased insignificantly, there was a significant decrease in the indices of endogenous intoxication, respectively, by 19.8% and by 24.3% (P <0.05).

Table no.4 Dynamics of endogenous intoxication of the oral fluid in patients with CRAS of the oropharyngial region with chronic cholecystitis after treatment

The studied indicators	Before treatment, patients with CRAS with chronic cholecystitis n = 54	After treatment patients with CRAS with chronic cholecystitis n = 54	After treatment patients with CRAS with with chronic cholecystitis n = 42
Average mass molecules E_{254} (conventional units)	0.381 ± 0.05 *	0.133 ± 0.02 *	0.078 ± 0.017 *
Average mass molecules E_{280} (conventional units)	0.419 ± 0.015 *	0.216 ± 0.002 *	0.102 ± 0.042 *
IL - 8 (pg / ml)	22.8 ± 1.63 *	3.63 ± 0.34 *	8.41 ± 1.01 *
Content of polymorphonuclear neutrophils (%)	76.7 ± 1.35 *	66.9 ± 3.11 *	69.2 ± 0.35 *

Note: * - P <0.05 significance of differences when comparing before and after therapy

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

Analysis of the percentage of PMNN in the examined individuals of the main group behind of complex treatment showed a significant decrease in 1.14 times, the level was 66.9 + 3.11% (P <0.05) (Table 4). In the comparison group, this indicator decreased by 1.1 times and amounted to 69.2 ± 0.35% (P <0.05).

We observed an increase in the level of IL-8 to values of 22.9 + 1.64 pg/ml in the examined patients with CRAS of the oropharyngeal region with chronic cholecystitis before treatment. When using the drug Baktizidim, there was a significant decrease in the level of IL-8 to values of 3.63 ± 0.34 * pg/ml (P <0.05), which is 6.3 times lower than the initial values. A slight increase in the level of IL-8 in the comparison group was revealed in the group who were using traditional treatment with Eludril, where the content of the pro-inflammatory cytokine IL-8 was 8.41 ± 1.01 pg / ml (P <0.05), which is 2, 7 times lower than the initial values (Table no.4).

Thus, the analysis of the obtained research results showed that the complex treatment of patients with CRAS of the oropharyngeal region with chronic cholecystitis with the use of Baktizidime, which acts on bacterial endotoxins and a probiotic Enterogermina leads to more pronounced positive biochemical changes in the studied parameters, compared with the biochemical parameters of patients with CRAS of the oropharyngeal region with chronic cholecystitis using Eludril in the comparison group.

Table no.5 Dynamics of complaints of patients with CRAS (days, M ± m) in groups

Symptoms	Light form		Moderate - severe form		Severe form	
	Main group, n = 18	Comparison group, n = 14	Main group, n = 18	Group comparison, n = 14	Main group, n = 18	Comparison group, n = 14
Pain	2.5 ± 0.73	5.39 ± 1.24 *	4.4 ± 0.2	7.83 ± 0.34 ***	6.42 ± 2.1	7.82 ± 0.39
Burning	3.5 ± 0.75	6.32 ± 0.38 **	5.6 ± 0.01	8.82 ± 0.41 ***	7.51 ± 0.1	10.38 ± 0.45 ***
The discomfort	7.2 ± 0.1	9.32 ± 0.39 ***	8.5 ± 1.6	10.46 ± 0.44	9.41 ± 1.4	13.51 ± 0.62 *
Hyperemia	3.5 ± 0.75	7.13 ± 0.28 ***	5.6 ± 0.01	8.32 ± 0.28 ***	7.51 ± 0.1	10.62 ± 0.33 ***
Edema	4.02 ± 1.2	7.20 ± 0.28 *	6.0 ± 3.2	9.26 ± 0.37	8.40 ± 1.6	12.72 ± 0.55 *
The beginning of epithelialization	3.3 ± 0.73	7.11 ± 0.23 ***	5.6 ± 0.01	9.26 ± 0.37 ***	7.9 ± 0.1	12.13 ± 0.52 ***
Complete epithelialization	7.6 ± 0.1	9.3 ± 1.28	9.4 ± 1.4	11.72 ± 1.4	10.3 ± 1.1	14.33 ± 0.71 **

Note: * - differences relative to the data of the main group are significant (* - P <0.05, ** - P <0.01, *** - P <0.001)

The dynamics of complaints of patients with CRAS of the oropharyngeal region with chronic cholecystitis in a comparative analysis showed that effective treatment in the main group contributes to the positive dynamics of regression of complaints of patients (Table no.5).

So, with a mild form of CRAS in the main group, there was no pain for 2.5 ± 0.73 days, in the comparison group with a mild form of CRAS, after the start of treatment, pain decreased by 5.39 ± 1.24 on days of observation. In the moderate-severe form of the main CRAS group, pain relief occurred within 4.4 ± 0.2 days, in the comparison group it occurred on days 7.83 ± 0.34. In the severe form of CRAS in the main group, the absence of pain after the start of treatment occurred within 6.42 ± 2.1 days, and in the comparison group, it occurred after 7.82 ± 0.39 days.

Decrease of feeling of burn is reliably observed in patients of the main group. So, after the start of treatment on days 3.5 ± 0.75, there is a decrease of feeling of burn in a mild form of CRAS of the main group, in the comparison group, a decrease in complaints of burning was observed on days 6.32 ± 0.39. A similar trend is observed in the moderate-severe form of CRAS; in the main group, after the start of effective therapy on 5.6 ± 0.01 days, in the comparison group, there was a decrease in the of feeling of burn by 8.82 ± 0.41 days (Table 5).In severe form, there was a decrease of feeling of burn, respectively, in the main group and in comparison by 7.51 ± 0.1 and 10.38 ± 0.45 days. Discomfort ceased to bother in the main group of mild patients on 7.2 ± 0.1 days after the start of complex treatment, in the comparison group, the patients showed regression of discomfort on day 9.32 ± 0.39. Patients who started complex treatment in the main group with moderate and severe forms of CRAS noted a decrease in discomfort by 8.5 ± 1.6 and 9.41 ± 1.4 days, respectively. In the comparison group, the dynamics of complaints of discomfort occurred within 10.46 ± 0.44 and 13.51 ± 0.62 days, respectively.

Signs of an inflammatory reaction, edema and hyperemia in patients with the main group of mild, moderate and severe forms of CRAS are significantly reduced by 3.5 ± 0.75 and 4.01 ± 1.2, respectively; 5.6 ± 0.01 and 6.0 ± 3.2; 7.51 ± 0.1 and 8.40 ± 1.6 days after the start of treatment. In the comparison groups, for all forms of CRAS, decreases by 7.13 ± 0.28 and 7.21 ± 0.28, respectively; 8.32 ± 0.28 and 9.26 ± 0.37; 10.62 ± 0.33 and 12.73 ± 0.55 days (table no.5).

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

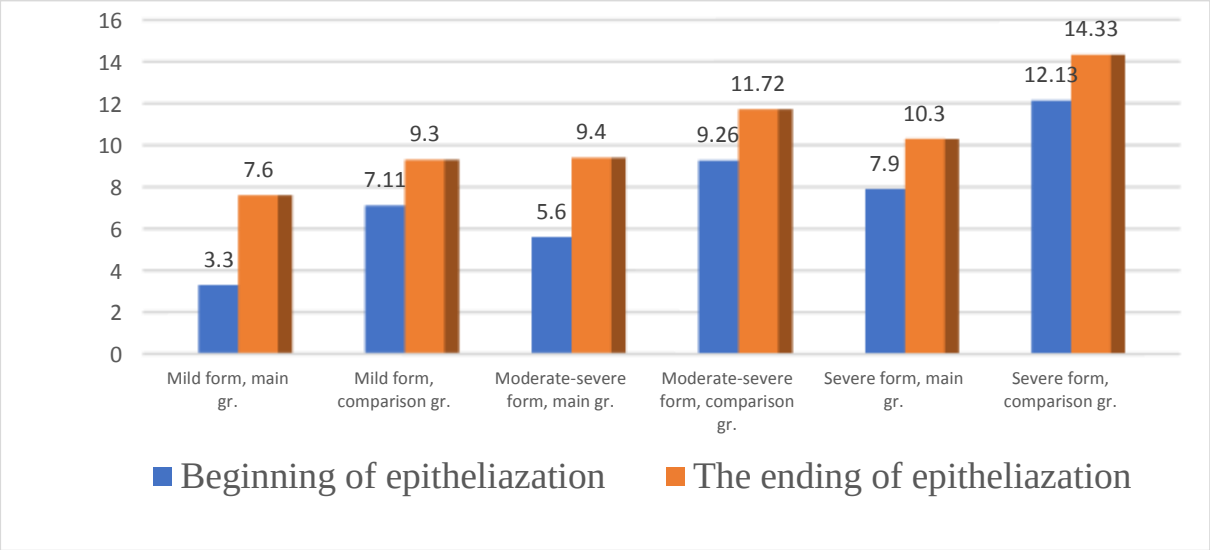

Figure: 1. The timing of epithelialization in the main and the comparison group patients with CRAS

The onset of epithelialization is observed in patients of the experimental groups with mild, medium-severe and severe forms of CRAS occurs at the time of regression of hyperemia and feeling of burn, respectively, by 3.3 ± 0.73; 5.6 ± 0.01; 7.9 ± 0.1 days, in the comparison groups, the positive dynamics of the onset of epithelialization in time, respectively, by 7.11 ± 0.23; 9.26 ± 0.37; 12.13 ± 0.52 days. Complete epithelialization in mild, moderate-severe and severe forms of CRAS occurs within 7.6 ± 0.1; 9.4 ± 1.4 and 10.3 ± 1.1 days, in the comparison groups a positive result was observed in the period of 9.3 ± 1.28; 11.72 ± 1.4; 14.33 ± 0.71 days (Fig. no.4).

Table no.6 Clinical evaluation of the results of treatment of patients with CRAS in the study groups

Effectiveness treatment	Light form				Moderate - severe form				Severe form			
	Main group n = 18		Comparison group n = 14		Main group n = 18		Comparison group n = 14		Main group n = 18		Comparison group n = 14	
	abs	%	abs	%	abs	%	abs	%	abs	%	abs	%
Remission	12	66.6	7	50.0	ten	55.6	6	42.9	nine	50.0	5	35,7
Significant improvement	6	33.3	4	28.7	7	38.8	6	42.9	7	38.8	4	28.5
Improvement	0	0	3	21.3	one	5.5	2	14.1	2	11.1	3	21.4
No effect.	0	0	0	0	0	0	0	0	0	0	2	14.2

WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979 (Volume 2, Issue 11, Nov., 2021

As can be seen from Table no.6, in patients with CRAS of all severity degrees, a high clinical result was recorded in the main group. Thus, in patients with a mild form of CRAS, remission was recorded in 12 (66.6%) patients; in the comparison group in 7 (50.0%), the corresponding ratios in patients with moderate-severe form were 10 (55.6%) versus 6 (42.9%); severe form in the main group in 9 (50.0%) versus 5 (35.7%).

The use of complex treatment in the main group with the use of Baktizidime led to a significant prolonging of remission. The average duration of remission in the main group was more than 12.88 ± 0.13 months, which is 1.69 times higher than in the comparison group - 7.60 ± 0.13 months (P <0.001); in patients with a moderate-severe form of CRAS it was 12.73 ± 0.26 months versus 8.41 ± 0.43 months (P <0.001), which is 1.51 times higher than in the comparison group; in severe form, respectively, 9.66 ± 0.33 months and 5.82 ± 0.23 months (P <0.001), which is 1.66 times higher than in the comparison group.

Thus, the frequency of relapses in patients with a mild form of the main CRAS group was 0.92 cases during 1 year of observation, in the comparison group 1.50 cases (decrease by 1.40 times) compared with the initial value before treatment. (p <0.05); in moderate-severe form in the study group, the recurrence rate was 1.71; in the comparison group 2.4 cases (decrease by 1.32 times) compared with the initial value(p <0.05) before treatment; in the severe form of the main group, the frequency of relapses respectively was 1.40 cases versus 2.6 (a decrease of 1.95 times) compared to the initial value(p <0.05) before treatment.

CONCLUSION

Our observations show that patients with a history of disease duration of more than 10 years have more severe forms of CRAS, with frequent relapses of the disease and are combined with background diseases, in particular, chronic cholecystitis. In this case, the aphthous-ulcerative elements of the lesion are often localized in the oropharyngeal region of the oral cavity, the tip of the uvula, palatine arches, and the soft palate.

With complex therapy with the inclusion of the drug Baktizidim, a significant decrease in endogenous intoxication of AMM was noted by 35% E_{254} and E_{280} - by 44% (P <0.05) in relation to the indicators before treatment, when compared with the group of healthy individuals, the decrease was respectively 1,6 times and 1.4 times. Analysis of the percentage of PMNN in the examined of the main group behind the complex treatment showed a significant decrease in 1.14 times, the level was 66.9 + 3.11% (P

<0.05). There was a significant decrease in the level of IL-8 to values of 3.63 ± 0.34 * pg/ml (P <0.05), which is 6.3 times lower than the initial values.

After complex pathogenetic treatment with the use of the drug Baktizidime in the main group, the average duration of remission in a mild form was 12.88 ± 0.13 months, which is 1.69 times higher than in the comparison group - (7.60 ± 0.13 months) (P <0.001); in patients with moderate-severe form it was 12.73 ± 0.26 months versus 8.41 ± 0.43 months (P <0.001), which is 1.51 times higher than in the comparison group; the severe form, respectively, 9.66 ± 0.33 months and 5.82 ± 0.23 months (P <0.001), which is 1.66 times higher than in the comparison group.

Literature

1. Azimboev N.B. Etiology and causes of chronic recurrent aphthous stomatitis of the oral cavity (literature review) / Young scientist. - 2016. - No. 26. - p. 189-193.
2. Banchenko G.V. Combined diseases of the oral mucosa and internal organs M.: Medicine, 1979. - p. 190.
3. Gabrielyan N.I., Lipatova V.I. Experience of using the indicator of average mass molecules in the blood for the diagnosis of neurological diseases in children // Laboratory work, 1984. -№3. p. 138-139.
4. Galizina O.A. The main aspects of the onset, clinical manifestations, treatment and prevention of chronic recurrent aphthous stomatitis / Clinical studies. RSJ, No. 6. 2014, p. 39-42.
5. Epishev V.A. Recurrent aphthous stomatitis / T. Medicine. 1968 p.72.
6. Ibragimova M.Kh. Tactics of diagnosis and treatment of diseases of the oral mucosa and periodontal disease in the pathology of the hepatobiliary system. Tashkent. Doctoral dissertation 2019. p.62.
7. Ibragimova M.Kh., Kamilova S.R. The state of microbiocenosis and local immune status of patients with CRAS in chronic calculous cholecystitis / Collection of articles Materials of the 5th International scientific-practical conference "Actual problems of dentistry". St. Petersburg, 2019. p.86-92.
8. Kamilov Kh.P., Ibragimova M.Kh. Evaluation of the effectiveness of complex treatment of patients with chronic recurrent aphthous stomatitis // Uzbekistan medicine journal. - Toshkent, 2016 . p.2-4.
9. Kosaeva Sh.K. Chronic aphthous stomatitis in the practice of a dentist-therapist. (Literature review) g. KazNMU Bulletin, No.1-2014, p.169-170.
10. Kosyuga S.Yu., Klenina V.Yu., Ashkinazi V.I. Analysis of the structure of concomitant general somatic pathology in patients with recurrent aphthous stomatitis / Modern problems of science and education. 2015. - No. 1 (part 1)

11. Languev A.I. Chronic recurrent aphthous stomatitis in the elder people. J. Clinical Gerontology, 9-10, 2015, p. 71.
12. Sidelnikova V.I., Chernitskiy A.E., Retskiy M.I. Endogenic intoxication and inflammation: sequence of reactions and informativity of markers. / Agricultural biology, 2015, volume 50, No. 2, p.152-160.
13. Uspenskaya O.A. Etiopathogenetic rationale for the treatment of chronic recurrent aphthous stomatitis with urogenital infection in background. / Abstract dissertation, 2015, p.32.
14. Ashwini Dhopte, Giridhar Naidu, Ramanpal Singh-Makkad, Ravleen Nagi, Hiroj Bagde, Supreet Jain. Psychometric analysis of stress, anxiety and depression in patients with recurrent aphthous Stomatitis-A cross-sectional survey based studyy / J Clin Exp Dent. 2018; 10 (11): e1109-14.
15. Borilova Linhartova, P., Janos, J., Slezakova, S., Bartova, J., Petanova, J., Kuklinek, P., Fassmann, A., Dusek, L., Izakovicova Holla, L. Recurrent aphthous stomatitis and gene variability in selected interleukins: a case – control study (2018) European Journal of Oral Sciences, 126 (6), p. 485-492.
16. Bryan J.W. Wong, Wa Sham Cheung and Karen M. Campbell. Aphthous stomatitis major in a 4-month-old infant / The Journal of Emergency Medicine, Vol. 55, No. 6, p. e157 – e158, 2018.
17. Chun-Pin Chiang and other. Recurrent aphthous stomatitis etiology, serum autoantibodies, anemia, hematinic deficiencies, and management/ Journal of the Formosan Medical Association Volume 118, Issue 9, September 2019, p. 1279-1289
18. Grimaux S., Leducq, P., Goupille A., Aubourg E., Miquelestorena-Standley M. Samimi. Ulcérations buccales aphtoïdes inaugurales d'une maladie inflammatoire chronique de l'intestin induite par le sécukinumab Aphthous mouth ulcers as an initial manifestation of sécukinumab-induced inflammatory bowel disease /Annales de Dermatologie et de Vénéréologie Volume 145, Issue 11, November 2018, p.676-682.