ABSTRACT

The Chronic Recurrent Aphthous Stomatitis (CRAS) is often described in practical work of the dentist [9,10,12, 13]. The disease wavy, sometimes with a frequent recurrence which severity and duration increase depending on prescription of a disease proceeds. Sometimes CRAS takes a permanent course. The problem of its treatment remains urgent [1,2,3,9,13]. The majority of the means of local therapy applied at CRAS are insufficiently effective, they are easily washed away by saliva and do not provide acceleration of an epitelization of the injured mucous membrane of oral cavity in short terms. This fact causes need of constant search for new medicine and its rational combinations [5,6,7,8].It is obvious that for effective damage therapy of oral cavity mucous membrane at CRAS it is necessary to use the medicines and substances allowed for use in medical practice with already known properties (for example, adhesive), as well as to develop and offer the new perspective means having universal properties [4,7,11].

In this regard studying the pathogenetic mechanisms of local therapy for damages of oral cavity mucous membrane of CRAS patients and developing the differentiated principles for this disease treatment, are an urgent problem of modern stomatology.

Keywords: mucous membrane, treatment, healing, stomatitis.

RESEARCH OBJECTIVE

To estimate efficiency of damage treatment for oral cavity mucous membrane for patients with chronic recurrent aphthous stomatitis when using new medicine.

Research materials and methods

For clinical tests 2 groups of patients - the main and control were created. 42 patients of the main group (22 women and 20 men) with the diagnosis of CRAS took part in clinical tests. Depending on degree of expressiveness of a disease clinical displays for patients with CRAS for local therapy we used the developed adhesive remedy (DAR), single damage are noted for 28 patients, multiple damage for 14 patients. In control group (12 patients) for local therapy we used Cholisal gel®. Besides, for receiving objective results for these biochemical researches, oral liquid and blood, in the group of 30 almost healthy people were tested. Composition of the developed adhesive remedy (DAR): glycerin, essential lavender oil of Kolosova, thyme ordinary, sage medicinal, peppermint, linden flowers, juice of a kalanchoe, two-blast furnace nettle, glycosamine hydrochloride, Polisorb-megapixel, pectin and dimethyl sulfoxide, at a certain ratio of components (the Russian Federation patent for the invention No. 2542469 of 20.12.2012) was applied. RALS represents uniform transparent gel, from light yellow till brown color with the pleasant grassy, refreshing mint, spicy smell. RALS is applied as follows: applied with a thin layer on the affected mucous membrane of oral cavity after each meal, by tooth brushing in the morning and in the evening. Objective assessment of clinical efficiency of the specified methods for local treatment was carried out by daily measurement of the damage area of oral cavity mucous membrane (aphthe and erosion) with use of amilliometric grid by formula: $S=m^21+m^22+m^23+m^24/n$, where $m^21$, $m^22$, $m^23$, $m^24$ - the sum of the areas of all erosion on the internal surface of cheeks (1), uraniscus (2), gums (3) and lips (4), n - the number of measurements. Efficiency of treatment was also estimated on disappearance of complaints from patients, aphthe epitelization speed, the remission period duration, definition of some biochemical indicators of oral liquid. The general treatment in all groups was identical and consisted in treatment of associated diseases, sanitation of oral cavity, elimination of the factors causing aphthe, the desensibilizing therapy (loratadine or centirizine). Research data are subjected to mathematical processing on the personal computer by means of statistical package Exel 2007, Statistica for Windous 5.0 programs. Results are presented in the form of average arithmetic and its standard error ($\bar{x} \pm m$). Reliability of distinctions ($r$) between values in each of groups was estimated for the different periods of time by

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means of Vilkokson's T-criterion (for comparison of the indicators measured in two different conditions on the same selection of test subjects). For comparison of two, three or more empirical distributions of the same sign we used $\chi^2$ - Pearson's criterion.

**Results And Discussion**

The results analysis of clinical observations showed that all patients in the presence in oral cavity aphthe did not carry out appropriate care of oral cavity as they were afraid to injure the mucous membrane, as well as because of aphthe morbidity that complicated hygienic care. Use of RALS improved a hygienic condition of oral cavity at CRAS patients that can be explained as direct antimicrobic action of components of the developed adhesive remedy, and their ability to stimulate salivation and increase local immunity.

**Clinical example. Patient T., 35 years, amb. card No. 1451 came to doctors with complaints for pain when opening his mouth, painful rashes on oral cavity mucous membrane which developed about 7 days ago, pain when swallowing, chewing and deep breathing. Right after emergence of rashes the health of the patient worsened sharply, body temperature indicators considerably raised to 38.5-39 °C, nonspecific signs of "the response to the sharp phase" - weakness, slackness, apathy, headache, dizziness, nausea and vomiting appeared. Meal and water consumption was limited. Objectively: Opening of a mouth is limited. On oral cavity mucous membrane, lips, palate and tongue characteristic elements of damage in a type of spots and aphthe with different degree of maturity are noted. On cheeks spots with the hyperemic center of oral cavity mucous membrane are noted, tongue and palate have an appearance of the ischemic site of a mucous membrane. Spots have the roundish and oval forms, are accurately delimited from unchanged tissues of oral cavity mucous membrane. Besides spots in oral cavity aphthe which have an appearance of the damage center of tissues integrity in the epithelium of a mucous membrane are noted (fig. 1).**

![Fig. (1). T. patient aphthe on a mucous membrane of a lower lip, corners of a mouth, an upper lip, cheeks](image)

When carrying out aphthe palpation, aphthe showed soft consistence and were also sharply painful. Around aphthe sites reddening was observed. On a aphthe surface the whitish raid which is rather densely connected to its bottom is visible. At an easy scraping the pallet on a surface of the aphthe does not come from a raid. In attempt of violent removal of a raid the aphthe bleeds. The greatest aphthe number is noted in the area of oral cavity threshold - in transitional folds, on the mucous membrane covering lips and cheeks in the area of the lower palate (fig. 2). At an aphthe palpation in the area of the basis infiltration, a hyperemic rim edematous is noted. Several large aphthe are noted on lobby and on side surfaces of tongue (fig. 2-b).
Fig. (2). Same patient. - multiple aphthe of oral cavity mucous membrane; - afta on a tip, side surfaces of tongue and in hypoglossal area
In a mucous membrane of cheeks damage have the rough and deforming character with formation of the hems which are formed after healing of defects in the form of more rough, volume, deep defects. Existence of such hems in oral cavity limits opening of a mouth for the patient with the microstomae phenomenon - sharp reduction of a mouth volume (fig. 3).

Preliminary diagnosis: chronic recurrent aphthous stomatitis. For specification of the made preliminary diagnosis of the patient are carried out: the general and biochemical blood tests, determination of blood glucose level, the general analysis of urine, allergic inspection with definition of the general and specific IgE, immunological researches, serological blood test (RW), blood test on antibodies to HIV. All specified research types allowed to establish the final diagnosis: the deforming form of chronic recurrent aphthous stomatitis. General treatment. To the patient the desensibilizing therapy, vitamin medicines (vitamins C, D, calcium a carbonate), plentiful drink is appointed. Local treatment: antiseptic processing, cleaning the aphthe surface mucous from the lifeless tissues by means of the pallet, as well as chemical way by means of fermental means, application of RALS 5-6 times a day. Treatment results: already on second day after application of the developed means the patient notes reduction of pain and reduction of the aphthe size on tongue and palate, with decreasing of symptomatology of “the response to sharp phase”. In 5 days after the beginning of RALS use the patient noted reduction of pain when swallowing, reduction of bleeding and the size of the centers of an ulceration on lips (fig. 4). In 7 days the patient does not show complaints. A hygiene index - 1,03 points (a good hygienic shape), a gingivo-parodontal index - 0,83 points (good shape of gums and parodont). The patient was on dispensary
observation 2 more months, did not show complaints. The obtained data confirm fast remission of disease right after the beginning of RALS use, acceleration of an epitelization of the injured mucous membrane of oral cavity.

![Image](image.jpg)

**Fig. (4). The same patient in 5 days after treatment initiation. Reduction of the aphthe sizes and ulcerations on a mucous membrane of an upper lip**

It is recommended to patient to adhere carefully during a recurrence to a diet with the use of not irritating food and drinks, to sanify oral cavity and the centers of chronic infection at least 2 times a year to undergo inspection at the stomatologist, in case of damage elements to use the developed adhesive remedy.

**Research results in groups of CRAS patients.**

Good adhesion of RALS allowed to use it on all surfaces of oral cavity mucous membrane on all patients of test group. When performing biochemical blood test for patients of test and control groups increase in quantity of histamine, amount reduction of protective enzyme of a lizotsim, as well as IgA as a part of oral liquid is established. It should be noted that the examined CRAS patients prior to treatment have a level of sialic acids, IGA and IgG, as well as value of coefficient of local immunity factors balance (Ksb) in oral liquid much higher, than in group of almost healthy persons. The analysis of levels of the general calcium, inorganic phosphorus, lizotsim and SigA, as well as activity of alkaline phosphatase as a part of oral liquid of patients in 5 days after initiation of RALS treatment and comparison medicine, confirmed their statistically reliable decrease to the levels comparable to the indicators revealed in group of almost healthy people. Increase in Ksb value for patients with CRAS found at a research of biochemical and immunological indicators of oral liquid prior to treatment emphasizes the fact of decrease in local immunity of a mouth cavity and protective function of oral liquid, reduction of alkaline phosphatase level in oral liquid, in turn, is connected with synchronization of an inflammation in oral cavity. It is known that in protective-adjustment reactions of an organism the most active part is taken by the general calcium and inorganic phosphorus defined at a research of biochemical and immunological indicators of oral liquid. As results of the carried-out analysis show, in the beginning at CRAS there is an increase in these indicators, then in process of disease developing, levels of calcium and phosphorus decrease that can be the basis for appointment calcium medicines to CRAS patients in a complex with colecalciferol. The biochemical data received during the research confirm much higher content of urea and uric acid at CRAS patients in comparison with group of almost healthy people (6,91±0,32 against 5,05±0,13 mol/l respectively, p <0,05), but the low level of creatinine (65,02 ±3,02 against 73,09±1,94 μmol/l respectively, p <0,05). Timolova test was higher (3,78±0,13 against 2,32 ±0,54 respectively, p <0,05), and levels a beta-lypoproteins and glucose are lower, than in group of almost healthy people (3,32±0,05 g/l and 3,54±0,15 mmol/l against 3,27±0,51 g/l and 4,22±0,14 mmol/l respectively). Levels of sialic acids were also higher than in group of almost healthy people - 701,11 ± 5,12 against 629,11±3,42 respectively. In 5 days after treatment initiation the studied biochemical indicators of blood for CRAS patients when using RALS, as much as possible approached similar indicators in group of almost healthy people (p <0,05) while for comparison medicine use this tendency only revealed in 7 days. The revealed increase in levels of the general protein in comparison with group of almost healthy people - 701,11 ± 5,12 against 629,11±3,42 respectively. In 5 days after treatment initiation the studied biochemical indicators of blood for CRAS patients when using RALS, as much as possible approached similar indicators in group of almost healthy people (p <0,05) while for comparison medicine use this tendency only revealed in 7 days. The revealed increase in levels of the general protein in comparison with group of almost healthy people is connected, probably, to the fact that at sharp inflammatory processes there is a strengthening of proteins synthesis of reply to sharp phase mediated by interleukin 1, 6, 8 to the
subsequent oncotic dehydrations of tissues. At chronic pathology there is an activation of immunological process and formation of immunoglobulins increases. Thus, the clinical tests made in the remote terms observations (in 1 year), showed that the number of recurrence a year for control group patients remained the same as before treatment - on average 4 times a year. In group where RALS was used, the number of recurrence decreased to 2 a year.

Conclusion
Application of CRAS in complex patient treatment of the developed adhesive remedies allowed to reduce considerably terms of epitelization elements of oral cavity mucous membrane damage - to 5-6 days (against 14-21 in control group).Thus, inclusion of the developed adhesive remedy in complex treatment of patients with chronic recurrent aphthous stomatitis promotes improvement of hygienic condition of oral cavity, elimination of the phenomena of a giposalivation, disbiosis and inflammation due to activation of oral liquid protective systems.

References