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CHANGES IN BIOCHEMICAL AND IMMUNOLOGICAL INDICATORS MIXED SALIVA OF PATIENTS WITH CHRONIC RECURRENT APHTHOUS STOMATITIS

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SUMMARY
The aim was a comparative study of the features of changes of biochemical, immunological parameters of peripheral blood and oral fluid in patients HRAS. It is established that patients with HRAS often observed regional lymphadenitis, Mikulich aphthosis, aphthae on different parts of the oral mucosa, mucosa swelling, high intensity of dental caries, periodontal index and integrated OHI-S index. There have been opposite changes the parameters of the immune system, indicating the presence of a chronic inflammatory process. When HRAS significantly more likely to occur hyperproteinemia, hypoalbuminemia, hyper-α-2-globulinemiya, increased ALT, AST, in the oral fluid marked decrease in activity of alkaline phosphatase, total calcium level, lysozyme and sIgA.

KEYWORDS: chronic recurrent aphthous stomatitis, mixed saliva, biochemical parameters, immunologic parameters.

Currently, there are sufficient data on the problem of investigation of chronic recurrent aphthous stomatitis (HRAS), including on the role of infectious factors in its development.[3,4]

There are neurogenic, immune, infectious and allergic theories of its origin.[1] Several authors have noted the importance of gastrointestinal pathologies in HRAS etiology.[3,5] Other scientists are inclined to favor the endocrine theory or the leading role of immunological reactivity and resistance of the organism.[6]

However, the etiology and pathogenesis of this disease are still poorly understood, and HRAS patients continue to suffer from frequent and difficult-to-treat recurrences. In addition, foreign scientists observed relapses HRAS often associated with provoking factors, including infectious nature.[2,4,6,7]

All of these issues now need to be addressed with the use of complex methods. Therefore, today there is a need to conduct a comprehensive study of HRAS with a detailed study of mixed saliva, the objective for the subsequent integration of data with the aim of developing modern principles etiopathogenical therapy of this disease.

Purpose of the research
Comparative study and evaluation of characteristics of changes in biochemical, immunological parameters of peripheral blood and oral fluid in patients HRAS.

MATERIAL AND METHODS
It carried out a clinical examination of 67 patients aged 25-35 years with HRAS residing in the Bukhara region of Uzbekistan. The control group included 14 healthy individuals of the same age and place of residence. Both groups were representative of each other, and all of the studies were randomized.

All patients studied was conducted complex hygienic and therapeutic-preventive measures that included sanitation, rational and professional oral hygiene.

Conducted a comprehensive evaluation of dental status: hygienic level determined under the simplified index hygiene OHI-S (Green JC, Vermillion JR, 1964). The intensity of the caries process was evaluated using KPU and index PA PEC Leus (1990), a comprehensive periodontal index (CPI) was also evaluated for Leus PA (1988), whereby the state of periodontal tissues examined.

Determination of serum immunoglobulin classes A, M and G (IgA, IgM, IgG) was performed by the method Manchini G. et al. (1965) using monospecific sera against IgA, IgM and IgG. Determined by the phagocytic activity of neutrophils (FAN) latex in combination with determination of phagocytic index Hamburger, circulating immune complexes (CIC) by the usual method. To determine the levels of α-interferon (IFNα) and tumor necrosis factor α (TNFα-TNF) was used ELISA method.

Used automatic biochemical analyzer "Mindray" to determine the biochemical parameters. The determination of blood fibrinogen Rutberg method. Unified method by reaction with acetic anhydride (method of Ilka) was used for determination of total cholesterol in blood serum. α-cholesterol was measured on CPK-2MP. Triglyceride levels in serum were determined by enzymatic colorimetric method with a set of reactants "triglycerides PS DDS" by ZAO "Deacon-DS" (Russia).

For the determination of bilirubin and its fractions in blood serum was used method of Endrashik (colorimetric method).

Alanine aminotransferase (ALT) was measured by method calorimetrically dinitrophenylhydrazine - Reitman-Frankel method using a set of the company "Lachema" reagents, and aspartate aminotransferase (AST) activity was determined by an optical test with an optimized use of the firm "Lachema" reagent kit.

The activity of serum α-amylase on aminoclastical method with resistant starch substrate (Karaveya method) using a set of the company "Lachema" reactants in serum levels of sialic acid was determined by the method of resorcinol. Huergo and Popper's method was used for thymol. content in serum β-lipoprotein was determined by turbidimetrical method of Burstein. Urea content was determined by using the «Diasys» reagent on a diacetylmonooxide method kit, creatinine color reaction Jaffe method. The content of uric acid in blood serum was determined by Trivedi modified Trinder, total calcium in blood serum of a photometric method using the set of the company "Lachema" reagents inorganic phosphorus by Fiske, Subbarow using a kit «Olvex Diagnosticum» reagents.

Determining the level of sialic acid in the oral fluid produced by Hess, alkaline phosphatase activity Besseya method, Lowry, Brock, total calcium amount by color reaction with o-kreozolftalein complex (o-ck); concentration of inorganic phosphorus by Fiske, Subbarow. Determination of secretory immunoglobulin (sIgA), IgG and IgA in saliva were determined by radial immunodiffusion in gel by Mancini (1965). Determination of lysozyme was performed using fotonefelometrical method.

Statistical analysis of the results was carried out using the methods of variation statistics on a personal computer using «Excel» applications.

RESULTS AND DISCUSSION
Research evidence that $80,6 \pm 4,8\%$ (n = 54) cases with HRAS patients reported discomfort, pain during eating and speaking. Moreover, these patients often observed following clinical manifestations: regional lymphadenitis ($80,6 \pm 4,8\%$, n = 54), Mikulich aphthosis ($77,6 \pm 5,1\%$, n = 52) for the simultaneous occurrence of aphthae different parts of the oral mucosa ($77,6 \pm 5,1\%$, n = 52) mucosal edema oral ($64,2 \pm 5,9\%$, n = 43) for the presence of "ulcers" in the oral cavity ($89,6 \pm 3,7\%$, n = 60), oral dryness ($6,0 \pm 2,7\%$, n = 4), hyper salivation ($56,7 \pm 6,1\%$, n = 38).

Total $37,3 \pm 5,9\%$ (n = 25) patients noted the presence of similar applications earlier, $62,7 \pm 5,9\%$ (n = 42) patients complaints occurred first.

The intensity of the pain depends mainly on the number of elements of destruction and localization. When viewed from the oral cavity aphthas have been discovered, soft to the touch, painful to palpation, located on hyperemic background spots covered with fibrous coating. At $53,7 \pm 6,1\%$ (n = 36) patients exhibited some swelling of the oral mucosa (GPRS), wherein the color was pale pink, at $46,3 \pm 6,1\%$ (n = 31) surrounding% GPRS has not been changed. At $47,8 \pm 6,1\%$ (n = 32) patients were observed 1-2 single aphthae 3-10 mm in diameter, at $53,7 \pm 6,1\%$ (n = 36) patients and 3 more sharply painful to touch aphthae with infiltration at the base and 5.11 mm in diameter.

In the analysis of dental status found that CPI was 1.96 ± 0.031, index OHI-S $2,14 \pm 0,06$ units, at $26,9 \pm 5,4\%$ (n = 18) patients were found to periodontal disease. The intensity of dental caries or KPU index was 10.81 ± 0.6 units. Patients HRAS constant K (caries) was equal to 3.78 ± 0.6, P constant (the sealed) $5,66 \pm 0,6$ (52%), have a constant (deleted) $1,37 \pm 0,04$. The level of intensity of caries (PEC) of the teeth was high in patients HRAS ($0,37 \pm 0,06$ units). KPI in the group of women with HRAS was equal to 1.96 ± 0.031, in the control group $1,83 \pm 0,023$ (p <0.05).

The results of the clinical analysis of blood revealed leukocytosis, lymphocytosis and monocytosis patients HRAS, indicating signs of chronic inflammation in patients.

On average, patients HRAS IgA and IgM content exceeded the upper normal value of the index parameter from $34,3 \pm 5,8\%$ (n = 23) women (p <0.05). The majority of patients HRAS observed immunological signs of chronic inflammation. Furthermore, the prevalence and severity of allergic and autoimmune manifestations in individual data groups was also significantly higher (p <0.001) compared to the control.

It is found that there is a positive correlation between the change in IgA and increased the number of circulating immune complexes (CIC) of greater than 90 units (higher than normal). In patients with an activated HRAS was defined test NST (with NBT), which makes it possible to determine the mechanism of oxygen-dependent bactericidal activity of phagocytes. Patients HRAS was found decline in activated NBT test in comparison with the norm (P <0.05).

Thus, in patients with HRAS indicators of immune system have been found, indicating chronic inflammation, as well as the preservation of the autoimmune process, as indicated by reduced FAN.

Determines the level of anti-inflammatory cytokines - TNF. There was a significant increase ($p < 0.05$) averages amount TNFa (50.8 ± 3.7 pg / ml) compared with values in healthy individuals (24.7 ± 1.3 pg / ml) - $p < 0.001$.

We noted a significant increase ($p < 0.05$) in patients with IgA content HRAS (2.3 times) and IgM (1.9 times) in the oral fluid when compared with a control group of patients (Table), furthermore revealed a significant decrease ($P < 0.05$) levels of inorganic phosphorus (3.1 times), silica acids (1.5), total calcium (8.4 times), alkaline phosphatase activity (1.5 times), the level of sIgA and lysozyme (respectively 3.9 and 3.6 times) - $p < 0.05$ $p < 0.001$.

Table. 1: Results of the study of biochemical and immunological parameters in patients with oral liquid HRAS.

Indicators of oral liquid	Control, n = 14	HRAS, n = 67
Inorganic phosphorus mol / l	8.23 ± 0.42	2.70 ± 0.39 *
Sialic acid units.	6.80 ± 0.18	4.50 ± 0.14 *
Total Calcium, mmol / 1	4.97 ± 0.39	0.59 ± 0.01 *
Alkaline phosphatase, mmol / 1 h	1.20 ± 0.03	0.82 ± 0.02 *
IgA, g / 1	0.07 ± 0.001	0.16 ± 0.001 *
IgM, g / 1	0.09 ± 0.001	0.17 ± 0.002 *
sIgA, g / 1	0.31 ± 0.08	0.08 ± 0.004 *
Lysozyme%	45.10 ± 2.4	12.42 ± 0.21 *

* - statistically significant differences with respect to control.

Determination results of the correlations revealed a close, direct relationship between the investigated immunological and biochemical parameters of oral liquid at HRAS. All of the above suggests the presence of violations of biochemical and immunological processes in the oral liquid at HRAS.

It found that at HRAS level of total protein, the percentage of α-2-globulins and γ-globulins were significantly increased, and the fractions of albumin, α-1-globulin and β-globulin was significantly reduced compared to the control. Increased levels of α-2-globulins in women with HRAS may be associated with inflammation, autoimmune and rheumatic diseases.

It is also noted that at HRAS patients' blood significantly increased liver enzymes - ALT and AST, acid phosphatase, while the level of α-cholesterol was significantly lower than in control subjects ($p < 0.001$). For HRAS typically increase the blood levels of total protein, which averaged 79.21 ± 1.3 g / L, which was significantly higher ($p < 0.01$) compared with control

group (70.92 ± 2.47 g /l), which is typical of inflammatory processes.

CONCLUSIONS
1. It has been established that patients with HRAS often observed regional lymphadenitis, Mikulich aphthosis, aphthae simultaneous appearance in different areas of the oral mucosa, swelling of the oral mucosa, a high level of intensity of dental caries, periodontal index and integrated OHI-S index.
2. It was found that patients with HRAS content of IgA and IgM exceeded the norm in 34.3% of women, prevalence, severity of allergic and autoimmune manifestations in these groups of individuals was also significantly higher compared to the control. A significant decrease activated NBT-test, FAN and increasing the amount of TNFa as compared with the norm.
3. HRAS significantly more ($p < 0.01$) occur hyper proteinemia, hypo albuminemia, hyper-α-2-globulinemiya, increased ALT, AST. When HRAS into oral liquid marked decrease in activity of alkaline phosphatase, total calcium level, lysozyme and sIgA.

REFERENCES
1. Bunny AS. Churilov LP. General pathophysiology of the basics of immunopathology// St. Petersburg, ELBI-SPb, 2005; 656 p.
2. Danilevskiy N.F. Diseases of the oral mucosa. //Moscow, 2001; 271 p.
3. Lukinykh LM. Diseases of the oral mucosa.// Nizhny Novgorod, NSMA, 2004; 351-357.
4. Rabinovich IM, Rabinovich OF, Panfilov EL, clothiers EV Recurrent aphthous stomatitis - etiology, pathogenesis (Part I) // Dentistry, 2010; 1: 71-74.
5. Rabinovich IM, Rabinovich OF, clothiers EV Recurrent aphthous stomatitis - classification and treatment of clinical forms (part II) // Stomatology, 2010; 3: 76-80.
6. Spitsina VI Features of immunodeficiency in patients with recurrent aphthous stomatitis // Russian Journal of Dentistry, 2006; (4): 14-17.
7. Assumption OA Features of hormonal levels in infertile women with chronic recurrent aphthous stomatitis // Basic Research, 2015; 1(Part 2): S.398-401.