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The Role of Iron in the Pathogenesis of Lichen Planus of Oral Mucosa

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Abstract

At present, the effect of deficiency or excess of various trace elements in the body on development and flow of chronic recurrent dermatoses, including lichen planus in oral mucosa, is studied. To study the role of iron in the pathogenesis of lichen planus of oral mucosa, its content in blood serum and saliva was determined in patients with lichen planus of oral mucosa. In patients with lichen planus of oral mucosa, the imbalance of iron content in serum and in oral fluid of pathological or adaptive nature was determined, which was of some importance in the pathogenesis of the disease. The interrelation between microelements' content in blood serum and in oral fluid and the clinical form and severity of the disease has been traced. With increasing severity of the clinical course, a significant decrease in the level of iron was observed mainly in the oral fluid, which in turn might aggravate severity of lichen planus of oral mucosa.

Key words: lichen planus, oral mucosa, minerals, iron, pathogenesis.

INTRODUCTION

Lichen planus is a chronic inflammatory disease of multifactor nature with diverse clinical manifestations, which involves skin, its adnexa (hair, nails) and mucous membranes. Many authors assign a leading role in development of the disease to disturbances in the immune system [1-4].

There are six clinical forms of lichen planus of oral mucosa (LP OM) and vermilion: typical, hyperkeratotic, exudative-rubefacient, erosive-ulcerative, bullous and atypical [5]. The erosive-ulcerous form of LP OM proceeds hard with pronounced exudative manifestations, formation of erosions or ulcers, frequent relapses. It has high risk of oncogenic transformation (in 0 to 3.5% of cases), accompanied by significant painfulness and torpidity, polymorphism of clinical manifestations and low efficiency of treatment [4, 6-8].

In the pathogenesis of inflammatory diseases, most important elements are changes in the hemato-tissue relationships aimed at recovery of disturbed homeostasis [9, 10]. Many hypotheses have been published about regulatory mechanisms of homeostasis by influencing transport of substances through the biological barriers. Under the action of various environmental factors faced by people in contemporary social and ecological conditions, most functional changes in the oral fluid are highly adaptive-compensatory in nature. Works of scholars have shown that determining the concentration of microelements has the important diagnostic value for detecting the systemic disease, even in the nonclinical stage [11-15]. The levels of macro- and microelements in the internal organs and environments show the homeostatic status of the organism; they are very accurate and sensitive criteria that may be a signal of pathological changes in it [6, 10, 16, 17].

To study the role of iron in the pathogenesis of LP OM, the content of microelement in serum and oral fluid was determined in patients with LP OM.

MATERIAL AND METHODS

Our study involved 191 persons with various forms of LP OM (43 patients with typical form, 43 patients with exudative-rubefacient form, 47 patients with erosive form, 24 patients with hyperkeratotic form, 28 patients with atypical form, 6 patients with bullous form); 30 patients without LP OM were the reference group. The elemental composition of blood serum and oral fluid was determined by atomic absorption spectrophotometry in the acetylene-air flame.

The data were statistically processed using the methods of biomedical statistics. For the purpose of finding quantitative indicators for choosing measures of central tendency, variation, tests for comparing group mean values, normality of distribution were performed with the use of the Kolmogorov - Smirnov method. In cases where the hypothesis of normality was taken, the arithmetic mean (M) was used as the measure of central tendency, and the standard deviation (δ) - as measures of variation. In cases when the hypothesis of normality was rejected, median (Me) was used as the measure of central tendency, and upper and lower quartiles (Q1 and Q3, respectively) were used as the measure of variation.

For comparing the group mean values in two groups for the indicators where the Kolmogorov-Smirnov test confirmed normality of distribution, the Student's t-test was used. With that, additional Levene's test was made for homogeneity of variances in groups and, depending on the result of this test, the corresponding modification of the t-criterion was chosen (t-criterion for the case of variances homogeneity, or t-criterion for the case of variances heterogeneity). To compare the group mean values in two

groups of the indicators, normality of which was rejected, the Mann-Whitney test was used.

To study the influence of several factorial indicators on the quantitative dependent indicator, the parametric variance analysis was used.

The power of factor influence denoted by symbol η^2 indicates the share (in %) of the effective indicator variability, which may be explained by the action of the same factor, or a combination of several factors. To assess the importance of influence of these factors on the productive indicator, the Fisher test was used.

RESULTS

For iron content in blood serum, the dependence of "group identity" factor turned out to be quite significant – η^2=40%, F=23, p<<0.0001).

There was a significant difference (Fig. 1) between the iron content in the blood serum in the reference group and those in groups with various forms of LP OM. With that, the average levels for "typical", "exudative-rubefacient", "hyperkeratotic" and "atypical" forms were almost identical (1,018 ± 25.2 µg/l, 1,019.7 ± 37.1 µg/l, 1,017.1 ± 15.1 µg/l, 1,021.6 ± 23.2 µg/l, respectively) and, accordingly, were not significantly different (p>0.72). In case of "erosive-ulcerative" and "bullous" forms of LP OM, the iron content in the serum was significantly higher and lower, respectively, than in other forms (1,059.5 ± 69.4 mg/l and 981.0 ± 33.5 µg/l). The fact of the significantly lower values of iron content in the blood serum in the bullous form of LP OM, as compared to other cases, was confirmed and compared by the Mann-Whitney test (p<0.02).

The iron content in the oral fluid varied in a completely different way. Dependency of this parameter on the factor of group membership "was very strong (η^2=94%, F=637, p<<0.0001). This dependency was generated by both the sharp difference between the reference group (416.4 ± 10.9 µg/l) and all groups with various forms of LP OM, and equally sharp differences between some of these groups (Figure 2). Noteworthy was the consistent and sharp (almost by one third each time) reduction of the iron content in the oral fluid from "typical" form of LP OM to the "exudative-rubefacient", and further to "erosive-ulcerative" (331.6 ± 17.1 µg/l, 251.8 ± 18.0 mg/l and 188.1 ± 11.0 µg/l, respectively). In case of "bullous" form of LP OM, the iron content in the oral fluid (190.2 ± 23.3 µg/l) was not virtually different from the same in case of "erosive-ulcerative" form (p>0.79). In case of "hyperkeratotic" and "atypical" forms, the content of iron in the oral fluid was similar (314.0 ± 13.3 µg/l and 321.7 ± 31.0 µg/l) and not significantly different (p>0.12).

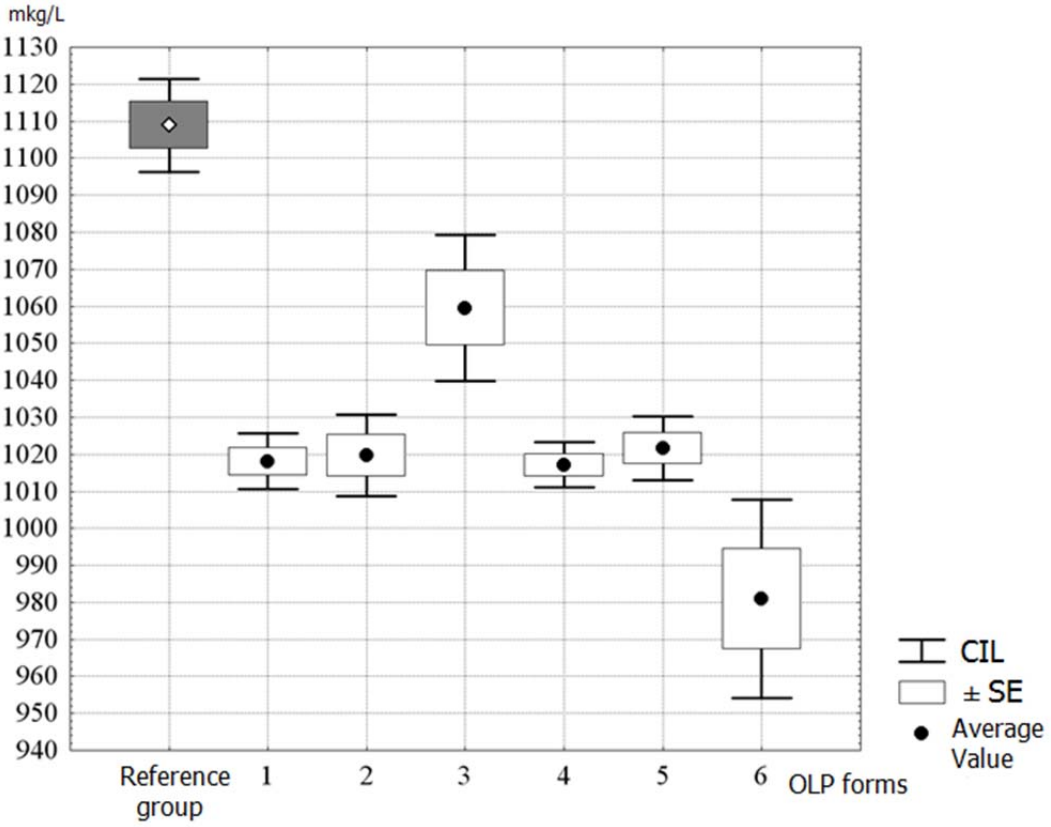

Figure 1 - Iron content in blood serum in patients with various forms of LP OM: Along the axis of ordinates - iron content in µg/L. Along the abscise axis – the reference group, forms of LP OM: 1 - typical form, 2 - exudative-rubefacient form, 3 - erosive-ulcerative form, 4 - hyperkeratotic form, 5 - atypical form, 6 - bullous form; CL – confidence limits for mean values, SE is the standard error of the mean value.

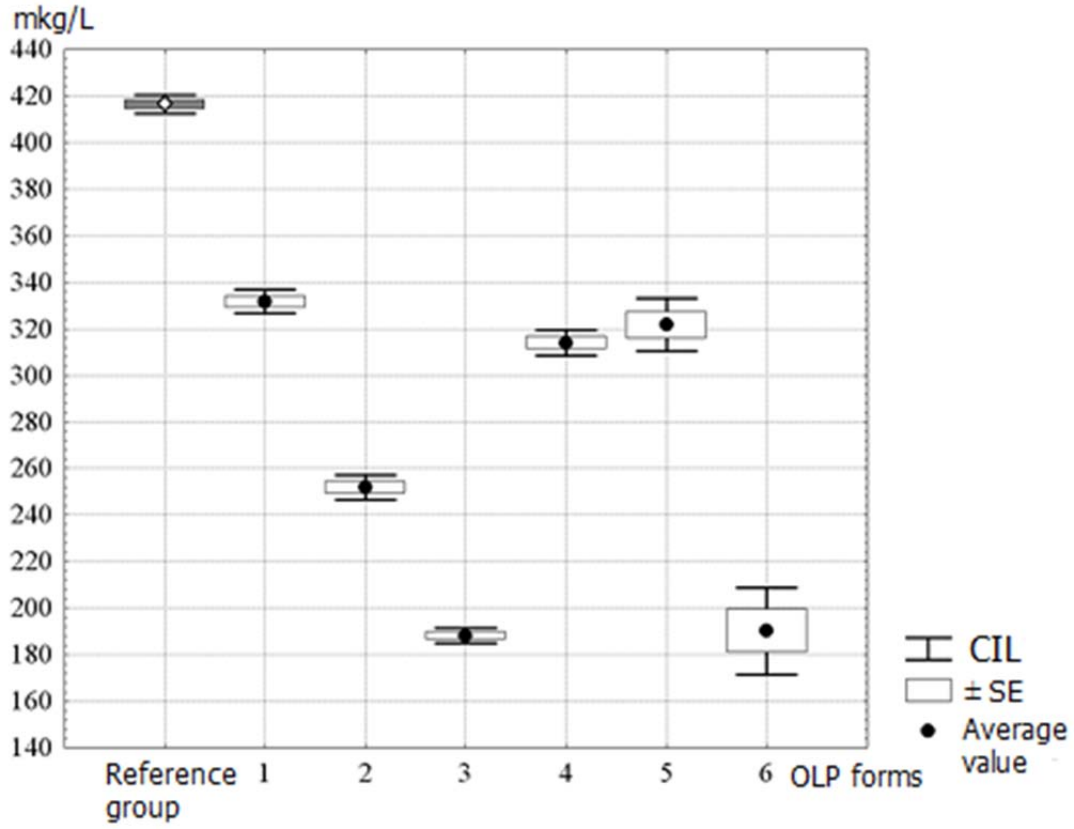

Figure 2 - Iron content in the oral fluid in groups of patients with various forms of LP OM. Along the axis of ordinates - iron content in µg/L. Along the abscise axis – the reference group, forms LP OM: 1 - typical form, 2 - exudative-rubefacient form, 3 - erosive-ulcerative form, 4 - hyperkeratotic form, 5 - atypical form, 6 - bullous form; CL – confidence limits for mean values, SE is the standard error of the mean value.

DISCUSSION

Microelements are essential catalysts for various biochemical processes, metabolism, and play a significant role in organism adaptation in the norm and in pathology. Many microelements are actively involved in plastic processes; therefore violations of the microelement status mainly affect the functional status of actively regenerating tissues (hematopoietic system, mucosal membrane of the gastrointestinal tract). Given the complex antagonistic and synergistic interaction and relationship between the elements, the clinical findings of microelementoses are often very difficult to interpret.

Iron in the organism is involved in many reactions of biological oxidation, and performs transport functions [18]. The reduced content of iron ions is apparently associated with its active use in the reaction of proline hydroxylation at the stage of post-translational modifications of collagen synthesis. Iron deficiency in the organism is accompanied by formation of a thin layer of epithelium, which is susceptible to environmental factors [6]. Ions of iron are also actively involved in the formation of the vascular bed, and its deficiency results in the increased vascular permeability and reduced vascularization of tissues. Consequently, the inflammatory response of the affected tissue subsides, and bridles are formed [6, 19].

As is well known, in case of iron deficiency, the clinical findings often show inflammatory and atrophic changes in mucous membranes, as well as immunodeficiency states. For iron, several antagonistic interactions with other minerals have been found - in case of excess of iron in the organism, copper and zinc deficiency may develop, while excess of zinc may, in turn, lead to copper and iron deficiency [18].

Attention should be paid to the fact that in our study, despite the significant changes in the content of the studied element in the blood, they did not exceed the generally accepted limits of reference values almost in all examined groups of patients with LP OM. Keeping in mind this fact, the found changes may be interpreted as pathological or adaptive disbalance of microelements, when their relative deficiency in blood, and especially in the oral fluid is formed in the conditions of actively flowing inflammatory processes.

CONCLUSION

With regard to the identified changes in the microelement status, the following may be stated: in patients with LP OM, the imbalance of iron content in blood serum and in oral fluid of the pathological or adaptive nature has been found, which is of some importance in the pathogenesis of the disease, and requires further study.

REFERENCES

[1] Suresh, S.S., Chokshi, K., Desai, S., Medical Management of Oral Lichen Planus: A Systematic Review. J. Clin. Diagn. Res, 2016; 10(2): ZE10-5.

[2] Di Stasio, D., Guida, A., Salerno, C., Oral lichen planus: a narrative review. Front. Biosci. (Elite Ed), 2014; 6: 370-376.

[3] Srinivas, K., Aravinda, K. and Ratnakar, P., Oral lichen planus - Review on etiopathogenesis. Natl. J. Maxillofac. Surg., 2011; 2(1): 15–16.

[4] Lavanya, N., Jayanthi, P., Rao, U.K. and Ranganathan, K., Oral lichen planus: An update on pathogenesis and treatment. J. Oral Maxillofac. Pathol., 2011; 15(2): 127–132.

[5] Akmalova, G. M., K voprosu ob atipichnoi forme krasnogo ploskogo lishaya na slizistoi obolochke rta [To the issue of the atypical form of lichen planus in oral mucosa]. The Urals medical magazine, 2013; 5 (110): 30-31

[6] Thongprasom, K., Novel therapies for oral lichen planus. J. Oral Pathol. Med., 2013; 42(10): 721-727.

[7] Romero, W., Giesen, L., Navajas-Galimany, L. and Gonzalez., S., Erosive lichen planus: a therapeutic challenge. An. Bras. Dermatol., 2016; 91(1): 84-6.

[8] Ribero, S., Stieger, M. and Quaglino, P., Efficacy of topical tacrolimus for oral lichen planus: real-life experience in a retrospective cohort of patients with a review of the literature. J. Eur. Acad. Dermatol. Venereol, 2015; 29(6): 1107-1113.

[9] Chuikin S. V., Akmalova G. M. and Slyshkina, T. V., Otsenka selektivnoi pronitsaemosti gematosalivarnogo baryera pri krasnom ploskom lishae slizistoi obolochki rta [Assessing selective permeability of the hematosalivary barrier in case of lichen planus of oral mucosa]. The Urals medical magazine, 2015; 6 (129): 104-107

[10] Chuikin S. V., Akmalova G. M., Gilmanov A. Z. and Gareev E. M., Sostoyanie pronitsaemosti gematosalivarnogo bar'era pri krasnom ploskom lishae slizistoi obolochki rta [The state of the permeability barrier of the hematosalivary barrier in case of lichen planus of oral mucosa]. Issues of dentistry, 2016; 12(1): 11-18.

[11] Gholizadeh, N., Mehdipour, M. and Najafi, Sh., Evaluation of the Serum Zinc Level in Erosive and Non-Erosive Oral Lichen Planus. J. Dent. (Shiraz), 2014; 15(2): 52–56.

[12] Sun, A., Lin, H.P., Wang, Y.P. and Chiang, C.P., Significant association of deficiency of hemoglobin, iron and vitamin B12, high homocysteine level, and gastric parietal cell antibody positivity with atrophic glossitis. J. Oral Pathol. Med., 2012; 41(6): 500-4.

[13] Chen, H.M., Significant association of deficiencies of hemoglobin, iron, folic acid, and vitamin B 12 and high homocysteine level with oral lichen planus. J. Form. Med. Assoc., 2015; 114(2): 124-129.

[14] Chin-Thin, W., Wei-Tun, C., Tzu-Ming, P. and Ren-Tse W., Blood concentrations of selenium, zinc, iron, copper and calcium in patients with hepatocellular carcinoma. Clin. Chem. Lab. Med., 2002; 40: 1118-22.

[15] Shelty, R., Babu, S. and Kumari, S., Role of serum trace elements in oral precancer and oral cancer – A biochemical study. J. Cancer Res. Treat., 2013; 1: 1-3.

[16] Hofman, L.F., Human Saliva as a diagnostic specimen. J. Nutr., 2001; 131: 1621-5.

[17] Ray, J.G., Ghosh, R. and Mallick, D., Correlation of trace elemental profiles in blood samples of Indian patients with leukoplakia and oral submucous fibrosis. Biol. Trace Elem. Res., 2011; 144: 295-305.

[18] Skalny A.V., Bioelementi v meditsine [Bioelements in medicine]. Moscow: Publishing House "Onyx 21 Century" – Mir, 2004.

[19] Zhang, Y., Lin, M. and Zhang, S., NF-kappaB-dependent cytokines in saliva and serum from patients with oral lichen planus: a study in an ethnic Chinese population. Cytokine, 2008; 41: 144–9.