Original Article

State Of C-Reactive Protein And Nitric Oxide In Blood Serum In Patients With Acantholytic Pemphigus

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Abstract

Resume

The article presents a study of the detectability of levels of C-reactive protein and nitric oxide B in the blood serum of 57 patients with acantholytic pemphigus. Patients with acantholytic pemphigus C have an increase in the level of nitric oxide C reactive protein by 3.8 times and nitric oxide NO B 2.1 times B in blood serum, which causes the severity of the inflammatory process due to the development of oxidative-nitrate stress in the body The indicator of nitric oxide in blood serum in patients with acantholytic pemphigus can be one of the criteria for assessing the dynamics of the clinical course of the disease and the therapy being carried out.

Key words: Acantolytic pemphigus, autoantibodies, C- reactive protein, endogenous intoxication, nitric oxide.

Introduction

Acantholytic pemphigus (AP) - is one of the severe dermatosis, accompanied by lesions of the skin and / or mucous membranes, the leading role in the pathogenesis of which is assigned to autoimmune reactions leading to the harmful effect of circulating auto-antibodies that are directed against the components of the desmosomes. [1-3]

In the development of the immune response, along with antibodies and cytokines secreted by lymphocytes, acute-phase serum proteins are also involved, the concentration of which rapidly increases during the infectious process. [4-12] It is known that any inflammatory process proceeds through a single system with the participation of general and local reactions, the course and nature of which depends on the reactivity of the organism, the state of the immune, nervous and endocrine systems. [13,15,18,21]

Thus, C-reactive protein is able to bind a wide range of ligands of microorganism components, toxins, and particles of damaged tissues, thereby preventing their spread. [18-21] Moreover, the binding of the C-reactive protein to the ligand on the cell surface, on the one hand, leads to bacterial opsonization and enhances phagocytosis, and on the other hand, activates the complement system. - The concentration of C-reactive protein in the blood serum increases with various inflammatory and necrotic processes and is an indicator of the acute phase of their course. It should be noted that the proteins of the complement system serve as mediators of phagocytosis, regulate the inflammatory response and, interacting with antibodies, participate in the immune defense of the body [14 17.20-25].

Recently, of great scientific interest is the study of the role of nitric oxide (NO), which is a universal transmitter in the development of various pathological conditions. According to studies, NO causes relaxation of vascular smooth muscles, participates in protection against pathogens, is a neurotransmitter, regulates programmed cell death and proliferation, and plays an important role in the secretory and reproductive systems. [Kuznetsova V.L., Solovieva A.G., 2015]

Nitric oxide has been found to be produced various cells in the body endotheliocytes, monocytes, fibroblasts, neurons. hepatocytes, mast cells and controls - they have many functions and biochemical processes epitheliocytes, mesangiocytes, myocytes, lymphocytes, neutrophils, platelets, macrophages, Nitric oxide acts as an inflammation mediator. Aseptic inflammation is associated with certain C isoforms of NOS.

In the early phase of the inflammatory response, under the action of mediators (histamine, bradykinin, prostaglandins and leukotrienes), nitric oxide production is stimulated by nNOS.

It was revealed that cNOS and iNOS are related to the production of nitric oxide in the early phase of inflammation.

Every phase The aim of our research was to assess the state of C-reactive protein in the blood serum of patients with acantholytic pemphigus.

Material research methods. We examined 57 patients with pemphigus aged 18 to 71 years. All patients underwent clinical, cytological, biochemical and immunological studies. Determination of the level of C-reactive protein in the blood serum was determined by the method of solid-phase ELISA research. (Vector-Best company). All patients were consulted by related specialists: therapist, endocrinologist, etc.

The control group consisted of data from 20 practically healthy individuals. To determine the concentration of nitric oxide, biochemical studies were carried out in the blood serum of 26 patients with AP. The level of NO was determined by the sum of metabolites of nitrates and nitrites (NO2 and NO3) according to the method described by P.P. Golikov et al. (2000).

Statistical results were processed research using statistically with standard methods of variation statistics using the application program "Excel-Office-2010" computer Pentium IV.

Research results. According to the clinical form, among 57 patients with pemphigus, the vulgar form was - 51 patients (89.5%), the seborrheic form - 4 (7.01%) and the vegetative form - 2 (3.5%), respectively.

The results of an ELISA study of the detection of C-reactive protein in patients with pemphigus showed that among 57 patients in 50 patients in the blood serum there was an increase in the level of CRP, which accounted for 87.7% of cases. In the group of healthy individuals, among 22 individuals, only one had an elevated level of CRP, which amounted to 4.5% of the case. (Table 1). The results obtained indicate the severity of the inflammatory reaction in the body of patients with sacantholytic pemphigus.

Table 1. The frequency of detection of C-reactive protein in the blood serum of patients pemphigus (abs, %)

№	Groups	Frequency of elevated CRP concentration	
		IU/l	
		*n	%
1	Patients with pemphigus N=57	50	87,7
2	Control healthy group N=22	1	4,5

Note: is the n- number of examined patients

* n is the number of detected elevated levels Analysis of the quantitative characteristics of the reactive protein (CRB) in the serum of the crowns of patients with pemphigus revealed an increase in concentration by 3.8 times compared with the control group and averaged 18.3±0.5 IU/ml and was statistically significant. (P<0.05).

Table 2. Indicators of the level of protein C-reactivity and nitric oxide NO in the serum of rabbits with pemphigus.(M+M)

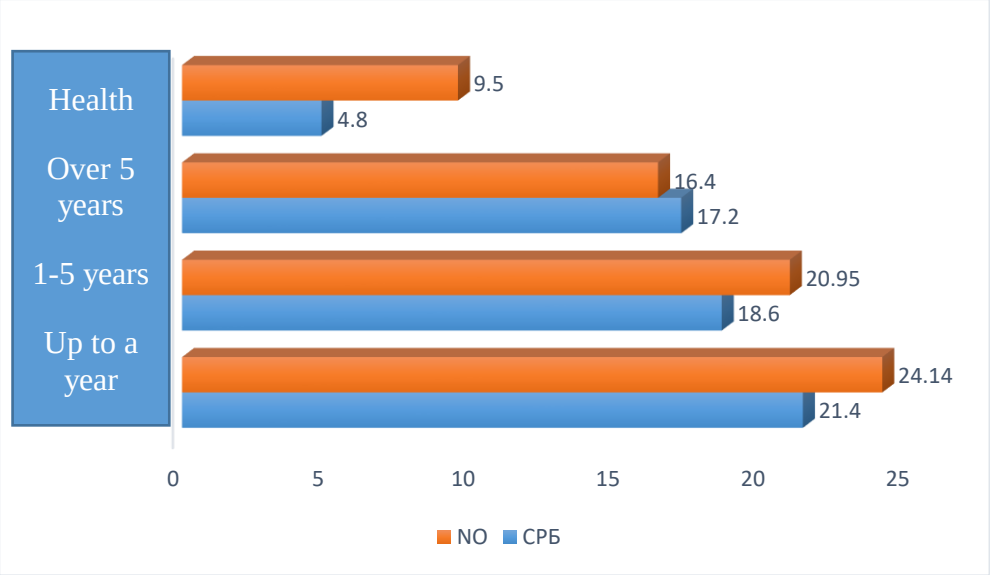
Indicators	**CRP (IU/mL)**	**Urea NO mmol/L**
Patients with true pemphigus N=57	18,3±0,5*	20,4± 0,64*
Healthy N=22	4,8±0,2	9,5 ± 0,31

Note: * - reliability indicator in relation to indicators of healthy individuals.

The data obtained were compared with the level of nitric oxide NO indicator, which characterizes the final production of endogenous intoxication.

The results of the biochemical method of research showed that in patients with AP in the blood serum there is an increase in the level of nitric oxide NO, X by 2.1 times compared with the indicators of healthy individuals, which averaged 20.4±0.64 mkmol/l (versus 9 .5± 0.31 mkmol/l - in healthy people). (P < 0.05)

The results were analyzed taking into account the duration of the disease. (Fig.1.).



Rice. 1. Indicators of CRP concentration (IU / ml) and nitric oxide (NO, mmol / l) taking into account the duration of the disease (abs)

As can be seen from Fig. 1, the level of C-reactive protein with a disease duration of up to 1 year averaged 21.4±0.6 IU/ml, with a prescription of 1-5 years - 18.6±0.8 IU/ml and more 5 years - 17.2 ± 1.3 IU / ml, respectively. (P<0.05).

A sharp increase in the level of CRP in patients with acantholytic pemphigus causes the initial stage of an acute inflammatory reaction of the body to the production of autoantibodies.

With an increase in the duration of the disease, the level of CRP is also in the range of high concentrations, however, compared with a prescription of up to 1 year, 1.2 times (P<0.05).

Whereas, the level of nitric oxide increased with the duration of the disease. Thus, in patients with AP with a prescription of up to 1 year, on average, it was 24.1 ± 0.5 μmol/l, which is 2.5 times higher than in healthy individuals (P <0.05). Whereas with a disease duration of 1-5 years, the level of nitric oxide averaged 20.9 ± 0.4 μmol / l and more than 5 years – 16.4 ± 0.4 μmol / l, which was 2.2 and 1.7 times higher than indicators of healthy individuals.

The data obtained were statistically significant. According to the literature data, under conditions of nigh concentrations of nitric oxide has a cytotoxic effect, promotes the development of the inflammatory process, damages DNA, inhibits mitochondrial respiration, enhances cell apoptosis and leads to persistent vasodilation, a state of hypotension and decompensation. Patients develops oxidative-nitrate stress.

As we can see from the figure, the nitric oxide index in patients with AP with a disease duration of 1-5 years and more than 5 years tended to decrease compared with a duration of up to 1 year. Such a decrease, in our opinion, is associated with the intake of a maintenance dose of hormonal drugs systemic of action.

However, the analysis of the content of nitric oxide in blood serum, taking into account causes of exacerbation of the disease showed that the level of NO remained at high rates compared with those of control healthy individuals. When the drug was discontinued, the NO level averaged 22.3+1.3 μmol/l, which was 2.3 times higher than in healthy individuals (p<0.05), in patients who had COVID-19 - 20.3±0 .4 and 2.1 times higher than in healthy individuals (P<0.05).

Whereas in patients with AP who could not specifically note the cause of the exacerbation, the level of nitric oxide was 22.1 + 1.0 μmol/l, which was also 2.3 times higher than in healthy individuals.

The data obtained were statistically significant. The data obtained indicate that patients with AP have a high concentration of nitric oxide NO by 2.1 times compared with the healthy control group. (P<0.05).

In our opinion, this phenomenon can be explained by the body's reaction to the production of autoantibodies and the exacerbation phase.

Analysis of the data obtained indicates that oxidative-nitrate stress develops in acantholytic pemphigus, which is expressed by an increase in nitric oxide and C-reactive protein in the blood serum, which determines the severity of the inflammatory process and the severity of the clinical course of dermatosis.

An increase in the level of nitric oxide, in our opinion, is a response to the development of the autoimmune process and the acute stage organism, AP patients. inflammatory process.

An increase in the level of CRP indicates the activation of autoantibodies, which contributes to the development of complications of both a bacterial and / or viral, fungal nature. In our opinion, the data obtained diagnostic and prognostic value of the clinical course of dermatosis, What B can be one of the criteria for assessing the adequacy of the therapy.

Conclusions:

1. In patients with acantholytic pemphigus, there is an increase in the level of nitric oxide C reactive protein by 3.8 times and nitric oxide NO by 2.1 times in the blood serum, which causes the severity of oxidative-nitrate stress due to the inflammatory development in the body. process,

2. An increase in the level of nitric oxide in the blood serum is the primary response to the developing autoimmune process and the acute stage of inflammation of the body in patients with acantholytic pemphigus. An increase in the level of CRP indicates the activation of autoantibodies, contributing to the development of complications, both bacterial and or viral, fungal in nature.

3. The indicator of nitric oxide in blood serum in patients with acantholytic pemphigus with can be one of the criteria for assessing the dynamics of the clinical course of the disease and the therapy.

Bibliography:

1. Abaturov A.E. The role of nitrogen monoxide in the system nonspecific protection of the body / A.E. Abaturov // Child health. - 2009. - No. 1 (16).

2. Abdurashidov A.A. Eczema bilan hastalangan bemorlarda endogen intoxication hysobga olib davolashning pathogenetic zhihatdan asoslanishi. Tib. fan. nomzodi ... dis. abstract. Tashkent, 2006. 186. 3. Adaskevich V.P. Diagnostic indices in dermatology. M: Panfilov Publishing House: BINOM. Knowledge Lab 2014; p.352.

4. Alekperov R.T., Baranov A.A., Abaitova N.E. Clinical associations of C-reactive protein in systemic scleroderma. Ter archive, 2006, 78 (6), 30-35

5. Gabrielyan N.I., Dmitriev A.A., Kulakov G.P. et al. Diagnostic value of determination of middle molecules in plasma in nephrological diseases. 1981. No. 10. pp.38-42. blood at //Klin. honey.

6. Kishkun A.A., Kudina A.S., Ofitova A.D., Mishurina R.B. The value of medium molecules in assessing the level of endogenous intoxication. // Military Medical Journal. 1990. No. 2. P.41-44.

7. Kubanov A.A., Znamenskaya L.F., Abramova T.V., Svishchenko S.I. - On the issues of diagnosis of true acantholytic pemphigus. Westdermatovenerol 2014; 6; pp.121-130.

8. Kuznetsova V.L., Solovieva A.G. Nitric oxide: properties, biological role, mechanisms of action.// Modern problems of science and education. - 2015. - No. 4

9. Imamov O.S., I.D. Complex therapy of patients with mycosis of the feet of older age groups// Ukrainian Journal of Dermatology, Venereology. cosmetology, No. 1 (44), 2012, p. 94-99

10. Nasonov E.L., Popkova T.V. Cardiovascular problems of rheumatology. Scientific and practical Rheumatology 2004;(4):4-9.

11. Nevskaya T.A., Novikov A.A., Aleksandrova E.N., Mach E.S., Zapryagaeva M.N., Speransky A.I., Gu N L. “Clinical significance of highly sensitive C-reactive protein in systemic scleroderma" / Scientific and Practical Rheumatology No. 4, 2007, p. 10-17

12. C-reactive protein in the development of atherosclerosis in women with lupus erythematosus system. Clinical Medicine 2006; 84(10):49−54

13. Togaibaev A.A., Kurguzkin A.V., Rikun I.V., Karibzhanova R.M. A method for diagnosing endogenous intoxication. //Lab.case. 1988. No. 9. S.22-24.

14. Yunonin I.E., Butusova S.V., Shilkina N.P. Markers of endothelial activation in systemic lupus erythematosus. Cytokines and inflammation 2011;(1):26−9.

15 Barnes E.V., Narain S., Naranjo A. et al. High sensitivity C-reactive protein in systemic lupus erythematosus: relation to disease activity, clinical presentation and implications for cardiovascular risk. Lupus, 2005, 14(8), 576-582.

16. BredaL., NozziM., De Sanctis S., ChiarelliF. Laboratory tests in the diagnosis and follow-up of pediatric rheumatic diseases: an update. SeminArthritisRheum 2010;40(1):53−72.

17. Decensi A, Omodei U, Robertson C, Bonanni B, Guerrieri-Gonzaga A, Ramazzotto F, et al. Effect of transdermal estradiol and oral conjugated estrogen on C-reactive protein in retinoid-placebo trial in healthy women. Circulation (2002) 106(10):1224–8. doi: 10.1161/01.CIR.0000028463. 74880.EA

18. Devaraj S, Du Clos TW, Jialal I. Binding and internalization of C-reactive protein by Fcgamma receptors on human aortic endothelial cells mediates biological effects. ArteriosclerThrombVascBiol (2005) 26:1359–63. doi:10.1161/ 01.ATV.0000168573. 10844.ae

19. Du Clos TW, Mold C. C-reactive protein: an activator of innate immunity and a modulator of adaptive immunity. Immunol Res (2004) 30(3):261–77. doi:10.1385/IR:30:3:261.

20. Eisenhardt SU, Thiele JR, Bannasch H, Stark GB, Peter K. C-reactive protein: how conformational changes influence inflammatory properties. Cell Cycle (2009) 8(23):3885–92.10.4161/cc.8.23.10068.

21. complement system I. Consumption of human complement associated with the reaction of C-reactive protein with pneumococcal C-polysaccharide and with the choline phosphatides, lecithin and sphingomyelin. J Immunol (1974) 112(6):2135–47.

22. Karadag O., Calguneri M., Atalar E., et al. Novel cardiovascular risk factors and cardiac event predictors in female inactive systemic lupus erythematosus patients. ClinRheumatol 2007; 26(5):695−9

23. Marnell L, Mold C, Du Clos TW. C-reactive protein: ligands, receptors and role in inflammation. ClinImmunol (2005) 117(2):104–11.10.1016/j.clim.2005.08.004.

24. Mold C, Gewurz H, Du Clos TW. Regulation of complement activation by C-reactive protein. Immunopharmacology (1999) 42:23–30.10.1016/S0162-3109(99)00007-7.

25. Mortensen RF. C-reactive protein, inflammation, and innate immunity. Immunol Res (2001) 24(2):163–76. doi:10.1385/IR:24:2:163

26. Tillet WS, Francis T. Serological reactions in pneumonia with a nonprotein somatic fraction of Pneumococcus. J Exp Med (1930) 52(4):561–71. doi:10.1084/jem.52.4.561

27. Trial J, Potempa LA, Entman ML. The role of C-reactive protein in innate and acquired inflammation: new perspectives. Inflamm Cell Signal (2016) 3(2):e1409.