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DYNAMICS OF INDICATORS OF THE PROOXIDANT AND ANTIOXIDANT BLOOD SYSTEM IN PATIENTS WITH PEMPHIGUS VULGARIS

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ДИНАМИКА ПОКАЗАТЕЛЕЙ ПРО- И АНТИОКСИДАНТНОЙ СИСТЕМЫ КРОВИ У БОЛЬНЫХ С ВУЛЬГАРНОЙ ПУЗЫРЧАТКОЙ

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The article presents the results of research on the dynamics of indicators of pro- (the level of malondialdehyde in erythrocytes and the level of average mass molecules in the blood serum) and the antioxidant system of the blood (the level of reduced glutathione in erythrocytes and the activity of ceruloplasmin in the blood serum) in patients with Pemphigus

Vulgaris (PV) of varying severity. The data obtained indicate significant shifts in the parameters of the pro- and antioxidant blood system in patients with PV, which correlated with the severity of the pathological process.

Keywords: pemphigus vulgaris, blood antioxidant system

Представлены результаты исследования динамики показателей прооксидантной (содержание малонового диальдегида в эритроцитах и молекул средней массы в сыворотке крови) и антиоксидантной системы крови (уровень восстановленного глутатиона в эритроцитах и активность церулоплазмина в сыворотке крови) у пациентов с вульгарной пузырчаткой различной степени тяжести. Полученные данные свидетельствуют о существенных сдвигах показателей про- и антиоксидантной системы крови у больных с вульгарной пузырчаткой, которые коррелировали со степенью тяжести патологического процесса.

Ключевые слова: вульгарная пузырчатка, антиоксидантная система крови

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AMM – average mass molecules
CP – ceruloplasmin
GSH – reduced glutathione
MDA – malondialdehyde
PV – pemphigus vulgar

Pemphigus vulgaris (PV) is a serious autoimmune disease with clinical manifestations in the form of exfoliating blisters on the skin and mucous membranes, including the oral cavity, where erosions remain after opening, causing incomplete mouth opening and unbearable pain [1].

The clinical experience of recent years indicates that PV is difficult to treat with traditional methods and means in most patients [2–5]. Despite the clinical, laboratory and experimental studies on PV problems conducted by domestic and foreign scientists, the issues of the etiology and pathogenesis of PV have not been fully clarified, which affects the effectiveness of the treatment [6–8].

In this regard, the search for alternative therapies that take into account changes in the oxidation and recovery processes in PV patients is relevant, as the study of the balance of programmable indicators and antioxidant blood system in patients allows for treatment of many diseases with prescription of pathogenetically based antioxidant drugs [9, 10].

The purpose of the study was to assess the predictive significance of the indicators of the pro- and antioxidant blood systems in patients with PV with different degrees of severity.

Material and Methods. In PV patients, the parameters of the prooxidant (the content of malondialdehyde (MDA) in erythrocytes and the content of medium-weight molecules in the blood serum) and antioxidant (the level of reduced glutathione in erythrocytes and the activity of ceruloplasmin in the blood serum) blood systems were determined. A total of 60 patients (main group) were examined, including 33 (55.0 %) men and 27 (45.0 %) women aged from 37 to 64 years with disease duration from six months until seven years. The control group consisted of 20 practically healthy individuals of the same age group. Patients with PV were divided into subgroups comparable in gender and age, depending on the severity of the disease: mild (n=20), moderate (n=26) and severe (n=14).

The MDA content in erythrocytes was determined as follows [7]: 2.5 ml of distilled water, 0.5 ml of $FeSO_4x7H_2O$ solution, and 0.5 ml of erythrocytes washed three times in isotonic NaCl solution were added to centrifugation tubes. The mixture was thoroughly stirred with a glass rod and allowed to stand for 10 min, after which 2 ml of 0.8 % thiobarbituric acid was added. The samples were stirred again, settled for 5 min, 0.6 ml of 60 % trichloroacetic acid was added, covered with foil, and placed in a boiling water bath for 10 minutes. After cooling, the samples were centrifuged for 10 minutes at a speed of 3000 rpm. The optical density of the centrifugate was determined at 532 nm in a 5 ml cuvette relative to the control (the same components as in the experiment, only 0.4 ml of distilled water was taken instead of erythrocytes: 3.6 ml of distilled water + 0.4 ml ($FeSO_4x7H_2O$) + 0.4 ml of water). The formula calculated the MDA content: MDA=E x 96.15, where E is the colorimeter indicator, and the MDA indicator was expressed in μmol/l of erythrocytes.

The standard method described by E. Beutler [11] was used to determine the level of reduced glutathione in erythrocytes (GSH). The determination is based on the interaction of GSH with 5.5'-ditio bis-2-nitrobenzoyic acid to form a yellow-colored anion 2-nitro-5-thiobenzoate. An increase in the yellow anion concentration during this reaction was observed spectrophotometrically at 412 nm. GSH levels in red blood cells were expressed in mmol/l.

The activity of ceruloplasmin (CP) in the blood serum was determined on a photoelectric colorimeter KFK-3 with a green light filter (530 nm) in cuvettes with a layer width of 10 mm. The results with the reference sample were compared. Ceruloplasmin activity was expressed in mg/l of plasma.

The research materials are mathematically processed on a personal computer with the help of statistical software packages Statistica for Windows 6.0. The Shapiro – Wilk criterion was used to determine the distribution, and the Student t-test was used for the normal distribution. With the help of the Studentt=test, the significance of the difference (p) between the values in control and the main groups is calculated; this criterion is used to estimate the difference between the values of the mean values of the two samples, which are distributed according to the normal law. The data were considered reliable at $p<0.05$.

Results and Discussion. The results of prooxidant and antioxidant blood system determination in the examined patients are presented in Table.

Table

Indicators of prooxidant and antioxidant blood systems in patients with PV

Indicators, units	Control group (n=20)	Main group (n=60)
MDA, red cells, μmol/l	4.45±0.22	8.64±0.58 p<0.05
AMM, blood plasma, c.units/ml	0.25±0.007	0.36±0.009 p<0.001
GSH, red cells, mmol/l	2.6±0.07	1.8±0.17 p<0.05
CP, blood plasma, mg/l	175.9±7.64	132.8±8.36 p<0.05

Note: p is the degree of significance of the difference in indicators relative to the control group.

Patients with PV show significant changes in the parameters of the prooxidant blood system of patients, regardless of their gender and age. A significant (p<0.05) increase (by 1.8 times) in the content of malonic dialdehyde in erythrocytes was found (p<0.05) as compared with similar indicators in the control group. At the same time, in patients with PV, an increase (by 26.4 %) (p<0.001) in the content of AMM in the blood serum, which are markers of endogenous intoxication of the patient's body, was found [9].

As can be seen from the Table, PV patients show reliable changes in the antioxidant blood system. Thus, PV patients have a reliable decrease (20.6 %) (p<0.01) in GBP, which is actively involved in oxidizing and reducing reactions of the body, in the neutralization of peroxides, xenobiotics, intermediate products of cellular metabolism [13]. Also, in PV patients, a decrease (25.4 %) (p<0.05) of CP activity – one of the non-specific factors of the antioxidant system is established.

The revealed changes in the parameters of the pro-oxidant and antioxidant blood system in PV patients as a whole are a reflection of the activation during the manifestation of the clinical manifestations of vulgar vesicle intoxication against the background of a decrease in GBP and insufficient CP activity, as an essential factor in antioxidant protection of the body.

To determine the degree of participation of oxidation and reduction processes in the pathogenetic mechanisms of development of vulgar bubble, the study of indicators of the prooxidant blood system in PV patients with different degrees of severity was conducted (light gravity, medium gravity, heavy current). The results of the indicators are presented in Figure 1.

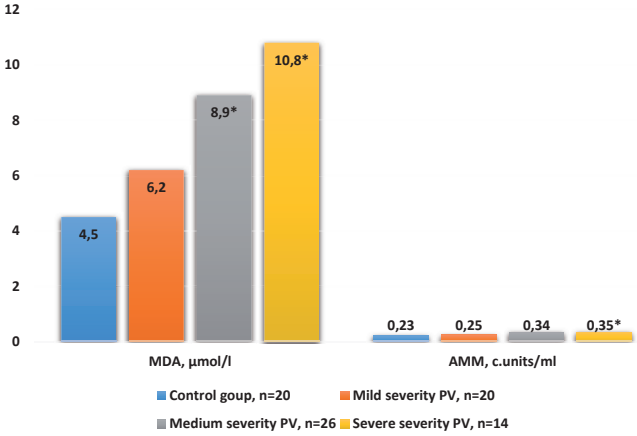

Fig. 1. Indicators of the prooxidant blood system in patients with PV of varying severity.
* – reliability of changes in indicators relative to the control group

As can be seen from the diagram, patients with mild PV showed a moderate increase in the prooxidant blood system, while patients with moderate to severe PV had reliable deviations. Thus, the MDA content in the erythrocytes of patients with light dermatosis was increased by 1.4 times, while in patients with moderate severity – by 1.9 times and in patients with a severe degree – by 2.6 times. A similar trend has been observed in the serum content of PV AMM patients. Thus, in patients with mild dermatosis, the AMM indicator was increased by only 8.7 %, in patients with moderate severity – by 33.6 %, and in patients with severe clinical flow PV – by 44.9 % (p<0.05).

The results of determining the indicators of the antioxidant system of the blood in patients with various forms of PV are shown in Figure 2.

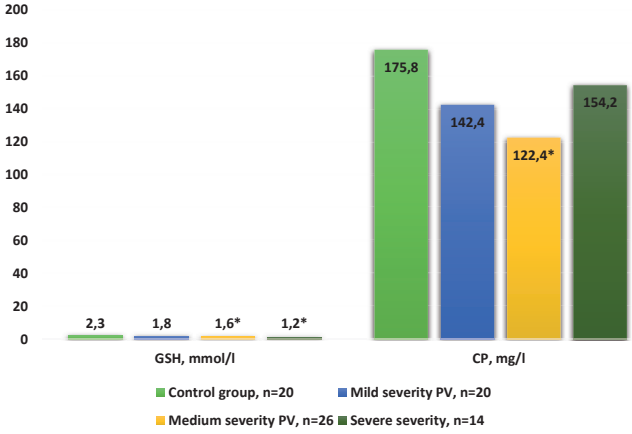

Fig. 2. Indicators of the antioxidant blood system in patients with PV of varying severity.
* – reliability of changes in indicators relative to the control group.

The presentation of antioxidant blood system data in PV patients of varying severity indicates their fuzzy nature. Thus, the GSH level in blood red cells tended to decrease gradually following the increasing degree of dermatosis severity. While in patients with mild PV, the GSH was almost the same as in the control group (a decrease of only 6.9 %), in patients with moderate PV, a reliable reduction of 20.4 % (p<0.05) was found in patients with a severe degree of clinical flow – its reliable decrease by 38.2 % (p<0.001).

CP activity in PV patients also varied depending on the severity of the disease. Thus, in patients with mild dermatosis, the CP activity rate was moderately reduced (by 18.3 %). In patients with moderate dermatosis, it was found to be significantly reduced – almost 1.5 times (a corresponding decrease of 44.6 percent, p<0.05).

In patients with severe PV, the CP activity indicator, in accordance with the indicators of the control group, only tended to decrease (by 12.8 %). In contrast, according to similar indicators, in patients with mild and moderate PV, its increase was noted (by 8.2 % and 26.9 %, respectively, p<0.05), which may be evidence of the activation of antioxidant protection in response to the growth of intoxication phenomena in patients with severe forms of PV.

In patients with severe PV, the CP activity rate according to the control group showed only a decreasing trend (12.8 %). In comparison, similar indicators showed an increase in patients with mild and moderate PV (by 8.2 % and 26.9 %, p<0.05), which may be evidence of increased antioxidant protection in response to increased intoxication in patients with severe forms of PV.

The conducted study allowed to note changes in indicators of the pro- and antioxidant blood system in patients with different degrees of severity of the clinical flow of vulgar bubble: a reliable ($p<0.05$) increase in erythrocytes MDA (1.8 times) and serum content AMM (26.4 %), as well as a reliable ($p<0.05$) reduction in GBP erythrocytes (by 20.6 %) and CP activity (by 25.4 %), which were dependent on the clinical form PV.

Currently, the literature provides data that indicate the pathogenetic significance in the development of bullous dermatoses of disorders of redox and membrane-destructive processes, which largely determine the processes that ensure the vital activity of both the cells themselves and the body as a whole [11, 12]. It is assumed that the indicators of the prooxidant blood system and antioxidant protection (activities of ceruloplasmin, catalase) can be criteria for assessing the effectiveness of patient treatment [13].

Conclusions. Analysis of the obtained data allows concluding significant violations of oxidation and recovery processes in patients with PV. The revealed changes in the parameters of the pro-oxidant and antioxidant blood system in PV patients were correlated with the severity of the pathological process, proving their serious importance in the pathogenesis of PV and the need for additional prescription of antioxidant agents for such patients.

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Informed consent. The study was conducted following the requirements outlined in the Federal Law of the Russian Federation of November 21, 2011, No. 323-FZ «On the Fundamentals of Protecting the Health of Citizens in the Russian Federation» and the Helsinki Declaration of the World Medical Association (as amended in 2013, Fortaleza), and a positive decision of the local ethics committee.

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