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IMMUNE RESPONSE REGULATORY DISORDERS AND REDOX HOMEOSTASIS IN PREGNANT WOMEN WITH ISOIMMUNE CONFLICT

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Abstract

The immunological and biochemical changes caused by pregnancy may uncover new aspects of immune tolerance, applicable in physiological and pathological contexts, and show up new therapeutic strategies for improving pregnancy outcomes. Isoimmune conflict in pregnancy is primarily related to the risk of pre-natal fetal death caused by massive hemolysis when incompatible with Rh and / or ABO antigens. The objective: The objective: to evaluate the role of redox homeostasis in the formation of the immune response in isoimmune conflict during pregnancy. Results. The results obtained indicate the activation of T- and B-lymphocytes, which may be explained by the activation of cytokines IL-1, IL-6, IL-10. In pregnancy isoimmune conflict moderate metabolic acidosis is observed with a predominance of the lactic acid component and the depletion of buffer reserves. Conclusions. Isoimmune conflict leads to moderate formation of oxidative stress, that can be described as violation of redox-homeostasis, which in turn can be a consequence of cytotoxic reactions.

Key words: isoimmune conflict in pregnancy; redox-homeostasis; cytotoxic reaction.

Introduction. Pregnancy causes a number of complex dynamic changes that accompany the approach of genetically inappropriate maternal and fetal tissues. Immunological aberrantism is the root cause of pregnancy complications, namely maternal-fetal conflict throughout pregnancy. Understanding of the immunological and biochemical changes caused by pregnancy may uncover new aspects of immune tolerance, applicable in physiological and pathological contexts, and show up new therapeutic strategies for improving pregnancy outcomes. Isoimmune conflict in pregnancy is primarily related to the risk of pre-natal fetal death caused by massive hemolysis when incompatible with Rh and / or ABO antigens [3; 5]. According to WHO experts, in economically developed countries the incidence of isoimmune conflict during pregnancy does not exceed 1 ‰, however, in some regions, much higher prevalence rates are present. Experts note higher incidence of isoimmune conflict among Caucasians compared to other races [1; 4]. Immunization of women with rhesus-negative blood can occur after the introduction of rhesus-positive blood into a woman's body, during pregnancy with fetus with rhesus-positive blood (regardless of the result of pregnancy: childbirth, involuntary, artificial abortion, ectopic pregnancy). Rh-immunization contributes to the violation of the integrity of the placental barrier (preeclampsia, threat of termination of pregnancy, extragenital pathology) and penetration into the bloodstream of the mother of fetal erythrocytes [2; 5]. Most often their transplacental transfusion is observed during childbirth, especially in complicated and operative births (manual separation of the placenta, caesarean section) [1; 3]. During the first pregnancy, 10% of women are immunized, if a Rh-negative woman has escaped Rh-immunization after the first pregnancy, then at a subsequent pregnancy, the Rh-positive fetus is at 10% of the risk of immunization [2].

Despite numerous studies of the pathogenesis of isoimmune conflict, it is still unknown just as the presence of acid-alkaline equilibrium, which causes oxidative stress and other disorders characteristic of acute hypoxia, affects the degree of immune disorders. According to current concepts, oxidative stress is an imbalance between oxidants and antioxidants due to the destruction of important indicators-signaling-control and / or damage to macromolecules. Preservation of the parameters of redox homeostasis is necessary for both individual cells and organelles, and for the body. It is also known that hemic hypoxia can induce the formation of biologically active compounds, which in turn induce the cytokine cascade, thereby affecting subpopulations of immunocompetent cells [3; 5].

The objective: to evaluate the role of redox homeostasis in the formation of the immune response in isoimmune conflict during pregnancy.

Research materials and methods.

The study was conducted on the basis of "Maternity Hospital No. 7" (Odessa) in the period 2011-2015. The main group consisted of 50 pregnant women with isoimmune Rh-conflict and 30 women with physiological pregnancy (control group) in the period 28-32 weeks of gestation. Surveys during pregnancy were conducted in accordance with the clinical protocol, regulated by the orders of the Ministry of Health of Ukraine (December 31, 2004 No 676 "On approval of clinical protocols on obstetric and gynecological care"; March 24, 2014 No. 205 "On amendments to the orders of the Ministry of Health Ukraine dated December 29, 2005 No. 782; December 31, 2004 No. 676). Comprehensive evaluation of the immunological profile was performed by flow cytometry based on the commercial laboratories "Sinevo" and "Dila", the assessment of redox homeostasis - electrochemical method at the clinical laboratory of KU "Maternity House No 7" (Odessa). Statistical analysis was performed by ANOVA analysis using Statistica 12.5 software.

Results of the study and discussion.

The most significant changes were observed in the subpopulations of CD3 + and CD19 + (Fig. 1).

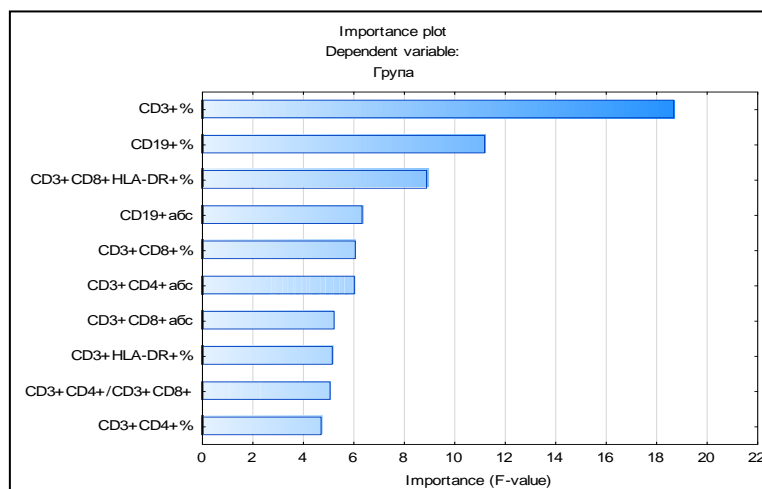


Fig. 1. The importance of indicators of cellular immunity by the results of the method "Feature Selection and Variable Filtering" module data mining (Data mining) in the graphic image: 1 — CD3+, %; 2 — CD19+, %; 3 — CD3+ CD8+ HLA-DR+, %; 4 — CD19+, a6c.; 5 — CD3+ CD8+, %; 6 — CD3+ CD4+, a6c.; 7 — CD3+ CD8+, a6c.; 8 — CD3+ HLA-DR+, %; 9 — CD3+ CD4+/CD3+ CD8+; 10 — CD8+ CD4+, %.

The results obtained indicate the activation of T- and B-lymphocytes, which, in turn, may be explained by the activation of cytokines IL-1, IL-6, IL-10 [2] and knowledge that moderate activation of reactions occurred in pregnant women of the main group. (Table 1). The described changes correlate with existing ideas about the pathogenesis of isoimmune conflict [2; 3].

Table 1.

The results of the analysis of variance in cellular immunity by One-way ANOVA in the studied groups of women (absolute values)

Indexes		Sum of squares	Degrees of freedom	The middle square	F	P
CD3+	Between groups	8.258	1	8.258	17.139	0.00001
	Inside groups	38.544	80	0.482	—	—
	In total	46.802	81	—	—	—
CD3+ CD4+	Between groups	3.851	1	3.851	11.137	0.001
	Inside groups	27.663	80	0.346		
	In total	31.514	81			
CD3+ CD8+	Between groups	0.653	1	0.653	6.652	0.012
	Inside groups	7.860	80	0.098		
	In total	8.513	81			
CD19+	Between groups	27.21	1	2.721	30.411	00.001
	Inside groups	7.159	80	0.089		
	In total	9.881	81			
NK	Between groups	0.011	1	0.011	0.072	0.789
	Inside groups	12.592	80	0.157		
	In total	12.603	81			

The above indicators correlated with the indicators of acid-base state of blood. In particular, in the main group the content of lactate was $(9,28 \pm 0,77)$ mg / l, and bicarbonates - $(20,53 \pm 0,28)$ mmol / l (Table 2). Thus, in isoimmune conflict during pregnancy, moderate metabolic acidosis is observed with a predominance of the lactic acid component and the depletion of buffer reserves.

Table 2

Indicators of acid-base state of blood in the studied groups

Group	Lactate, mg / l	Bicarbonates, mmol / l
Main	9.28±0.77*	20.53±0.28*
Controle	6.24±0.78	22.27±0.59

Note.* - statistical significance of differences with controls (p <0.05).

Conclusions:

In isoimmune conflict, activation of a subpopulation of T and B lymphocytes is observed. This state may be associated with an increase in antigen presentation.

Isoimmune conflict leads to moderate formation of oxidative stress, that can be described as violation of redox-homeostasis, which in turn can be a consequence of cytotoxic reactions.

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