

Immunological changes in HIV-positive pregnant with associated herpes-infection

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An analysis of the clinical course of the first half of pregnancy in HIV-infected patients and women with HIV-associated HSV infection is considered in the article. It is shown that along with inherent to the HIV-infected pregnant high incidence of infectious gestational complications studied group also had a significant risk of miscarriage. Features interleukins' balance dy studied pregnant women and their importance in the development of gestational complications are discussed.

Key words: HIV infection, herpes infection, gestational complications, interleukins.

Infection caused by the human immunodeficiency virus (HIV) through rapid growth and spread of lesions reproductively active segment of the population is of great interest researchers and practitioners with regard to issues of pregnancy, childbirth and infant period. One of the medical and social characteristics of HIV have a high propensity to mix with other diseases, sexually transmitted infections in the first place – with herpes simplex virus (HSV). Inherent HIV suppression of cellular immunity contribute atypical herpes infections (HI), the formation of short remission period. However, gestational changes contagious resistance, in turn, contribute to frequent and prolonged exacerbation of HI, which increases the risk of various complications of pregnancy, childbirth and the postpartum period.

The aim of the study was to investigate the clinical and immunological features of the course of gestation in pregnant women with HIV-associated HSV infection.

MATERIAL AND METHODS

Pregnancy period and complacitions of 54 pregnant women with HIV-associated HSV infection (I-study group), 86 pregnant women with diagnosed HIV infection without clinical and laboratory manifestations of HI (II group – comparison group) and 50 healthy pregnant women (III – control group). To study pregnant women with gestational period 24–28 weeks were included. Research conducted at the Kyiv City Center for Reproductive Medicine, the inclusion of pregnant women in the study met all the requirements of anonymity and obtained informed consent of women.

Through careful study of medical papers the incidence of complications during pregnancy, as threatened miscarriage, toxemia first half of pregnancy and preterm delivery, preeclampsia, anemia and infectious complications among all patient groups were registered. In addition, all pregnant women included in the study investigated the concentration of pro-and anti-inflammatory cytokines in serum by enzyme immunoassay. For IL1 normal values determined by laboratory data from 10 to 50 pg/ml, for IL-4 – 1,0–35 pg/ml, for IL-6 – 5,0–50,0 pg/ml, for IL-10 – 1,0–45,0 pg/ml. Because of the large range of reference values pregnant were surveyed distributed according to the principle: normal, reduced and elevated levels of the class IL.

A laboratory part of the research was performed at the laboratory «Eurolab». Statistical processing of the results obtained by use of the criterion of angular transformation and calculating of the coefficient of Student.

THE RESULTS AND THEIR DISCUSSION

The pregnancy by HIVinvecion has traditionally been considered as having an increased risk of infectious complications. So among patients of I and II group more often were manifestations of acute viral respiratory infection (ARI) – almost every second. The reason for this is the destruction of T-helper immunity infected pregnant women, what is the mechanism that is responsible for identifying new viral agent for the body (such as influenza virus and other respiratory viruses, which are characterized by high variability) and the stimulation of B cells to specific antibodies synthesize. This mechanism explains the proper and high susceptibility to infection by HSV lesions. The high frequency of opportunistic infections is nonspecific in pregnant women infected observed Dhanasekar G. et al. (2006).

In addition to viral infections, HIV-infected patients are more likely to develop infectious complications such as gestational pyelonephritis.

The frequency of genital herpes lesions should be noted. As it was proposed by design of study, patients with the manifestation of HI during this pregnancy were not included to the II group. In the same time, all I group patients have had typical

Complications of the first half pregnancy in examined patients

Table 1

Gestational complication	I group, n=54		II group, n=86		III group, n=50	
	Abs.	(%)	Abs.	(%)	Abs.	(%)
The threat of miscarriage	26	48,1*	16	18,6	6	12,0
Vaginal bleeding	19	35,2*	19	22,1*	4	8,0
Nausea and vomiting	19	35,1	24	27,9	17	34,0
Anemia	34	62,9*	54	62,8*	9	18,0
ARI	27	50,0*	35	40,7*	8	16,0
HH manifestations	54	100	-	-	5	10,0
Pyelonephritis	10	18,5*	17	19,7*	2	4,0

Note * – $p \leq 0,05$ when compared with the control group.

Distribution of pregnant women surveyed by the concentration of different classes of cytokines

Cytokine concentration in plasma	I group, n=54		II group, n=86		III group, n=50	
	Abs.	(%)	Abs.	(%)	Abs.	(%)
IL-1						
Normal	10	18,5	6	6,9*	10	20,0
Increased	12	22,2	67	77,9*	5	10,0
Reduced	32	59,3	13	15,1*	35	70,0
IL-6						
Normal	13	24,1	10	11,6	7	14,0
Increased	18	33,0	63	73,3*	10	20,0
Reduced	30	55,6	13	15,2	33	66,0
IL-4						
Normal	12	22,2	19	22,1	16	32,0
Increased	10	18,5*	23	26,7*	29	58,0
Reduced	32	59,2*	44	51,6*	5	10,0
IL-10						
Normal	19	35,1	24	27,9	14	28,0
Increased	13	24,1*	22	25,6*	27	54,0
Reduced	22	40,7*	40	46,5*	9	18,0

Note. * – $p \leq 0,05$ when compared with the control group.

rash on the genitals during this pregnancy, those herpes origin was confirmed by PCR. However, in the control group 5 pregnant women (10.0%) had complaints of herpes rash during this pregnancy. This indicates the provoking role of the gestation process in development of acute htrpes, consisting mainly of typical changes in immunity and nonspecific antiviral it's parts.

Besides the risk of infectious complications, pregnancy by HSV-associated HIV infection had other features. Thus, the threat of miscarriage occurred in 48.1% of women in Group I, that is significantly higher than in the third group. To some extent this can be explained by significant nerve stress that his patients experienced a part of the main group and the comparison group, learning about HIV status. However, the threat of miscarriage with vaginal bleeding is difficult to explain only the emotional stress, because this requires a deeper involvement of pathogenic mechanisms.

It should be noted that the patients of group pointed to the threat of miscarriage during this pregnancy were twice as likely than HIV-infected patients Group II. This can be explained by the specificity of the immune resistance inherent in pregnancy - for the development of heterogeneous half fetus in pregnant observed phenomenon of inhibition of cellular immunity. Paradoxically, in HIV-induced cell defect level for the development of early pregnancy period created an immunological point of view favorable conditions. High frequency of threats to abortion against secondary infections in patients of Group II is caused by activation of humoral immunity, release of proinflammatory cytokines and prostaglandins cascade activation [1].

Very often the patient group and were instructed to vaginal bleeding, which was accompanied by a threat of miscarriage, which may have a direct causal factor for vascular lesions chorion virus.

Nausea and vomiting were registered in all 3 groups with equal frequency, a slight tendency to increase in the second group has no statistical significance. It should be noted that the formation of complaints of nausea and vomiting in pregnancy I-II groups could be affected by specific antiretroviral therapy.

Among the gestational complications that were found HIV, one of the leading places takes anemia. It was found in 62.9% of pregnant women of I group and 62.8% – the second group. By dates of E.Yu.Stepanova (2010), anemia in HIV-infected people is an essential factor that adversely affects the character of the disease. Among the reasons that may cause anemia in HIV-infected pregnant women, besides the typical gestational iron deficiency, there is a specific infectious-associated ones - the impact of the virus on the bone marrow, the effect of opportunistic infection with activation of cytokine cascade, as well as side effects of antiretroviral therapy. Among the methods for correcting iron deficiency author emphasizes the role of stabilization of immunity, especially – viral load meaning.

Thus, pregnancy by HSV-associated HIV infection had a number of clinical features, the causes of which lie in the peculiarities of the immune response by 3 parallel factor – HIV, HSV and actual pregnancy, their mutual resurface. Some differences were found at the level of distribution pregnant for the balance of cytokines that is presented in Table 2.

Cytokines are known to play an important role in the processes of cooperation and specialization immune-active cells, respectively, in the implementation of an adequate immune response. Today the role of cytokines is not limited to their participation in inflammatory and immune reactions. Cytokines regarded as transmitters involved in the association and the formation of functional unity of the major regulatory systems – immune, nervous and endocrine. Particular value cytokines becomes during pregnancy because it is only through the interaction of trophoblast and decidual cells, providing tolerance between the mother and fetus.

Interleukin (IL) is a subclass of cytokines that are primarily engaged in the interaction between leukocytes. According to the modern nomenclature, IL divided into a group of proinflammatory and anti-inflammatory, depending on their role in the inflammation regulation. The first group includes IL-1 and IL-6, the second – IL-4 and IL-10.

In study has been shown, the ratio of proinflammatory and anti-inflammatory interleukins orientation differed among pregnant

women of different groups. Thus, the group of physiological pregnancy in determining the level of cytokines in term of 24 weeks revealed the predominance of the concentration of anti-inflammatory subtype mediator. This distribution of cytokines during pregnancy is natural and is the fraction of relative immunosuppression.

II group of pregnant distribution by type cytokine concentration was the opposite - the overwhelming majority of HIV-infected pregnant women had increased concentrations of proinflammatory cytokines, indicating partial activation of the immune system, which is characteristic of the first stage of the disease. Thus, among the patients and 77.9% of pregnant women had a higher concentration of IL-1 and 73.3% – IL-6.

This high content of proinflammatory cytokines in the pathogenesis and appropriate group surveyed, can cause threats to abortion (which took place among them in 41.9% of cases). Proinflammatory IL-1 is a central mediator of local and systemic inflammatory reactions. It's transcription is stimulated by cell wall of bacteria, components of complement, and other cytokines. At early terms of pregnancy high concentration of IL-1 is a prerequisite for normal implantation because it enhances adhesive properties of trophoblast. However, after a process of implantation in physiological conditions, a decrease in the concentration of IL-1 is casual, that is confirmed by results of control group. Increased concentration of IL-1, it found only in pregnant women in I group due to nonspecific immune defense, activated HIV.

IL-6 also belongs to the pro-inflammatory cytokines that is secreted by trophoblast. Along with all the attributes of proinflammatory IL, including activation of arachidonic cascade, regulation of hemostasis, IL-6 is able to enhance the expression of oxytocin receptors in myometrium, increasing prostaglandins induced premature birth activity. That is why in the first group of pregnant women was predicted premature labour, additional pathogenic stimulus for which could be any adjacent inflammatory process that took place, particularly in 19.7% of women in the form of pyelonephritis and in 40.7% of cases in the form of ARS.

Імунологічні зміни у ВІЛ-позитивних вагітних із супутньою герпетичною інфекцією

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У статті наведено аналіз клінічного перебігу першої половини вагітності у ВІЛ-інфікованих пацієнток та жінок із асоційованою ВІЛ-ВПГ-інфекцією. Показано, що поруч із притаманною ВІЛ-інфікованим вагітним високою частотою інфекційних гестаційних ускладнень, досліджувана група мала також значний ризик невиношування. Вивчено також особливості балансу інтерлейкінів у обстежених вагітних та їх значення у розвитку гестаційних ускладнень.

Ключові слова: ВІЛ-інфекція, герпетична інфекція, гестаційні ускладнення, інтерлейкіни.

As for the second group of pregnant women, they have seen a steady decrease in the concentration of proinflammatory cytokines (62.4% of patients in this group had a lower concentration of IL-1 and 59.6% – IL-6). This reduction in cytokine level of antiviral protection is considered one of the turning points in the development of AIDS caused uploads and development of opportunistic infections.

Analysis of the distribution of pregnant women over the concentration of anti-inflammatory cytokines is also found differences between the groups. Thus, I group of pregnant is pointed by mainly reduction of anti-inflammatory IL-4 (46.5%) and 10 (62.8%), due to nonspecific activation of the immune system origin. However, in the second group of pregnant women found the same probable tendency to reduction of inflammatory cytokines that distinguishes it from the control group surveyed (58.7% – IL-4 and 41.2% – IL-10).

IL-10 is a major protective cytokine pregnancy that is expressed in the endometrium and placenta T2 class cells, reducing of its concentration is proper to women after abortion. IL10 with IL4 involved in the preparation of the endometrium for implantation, providing local immunosuppression by limiting the activity of normal killers, macrophages, expression of steroid hormone receptors. Physiological pregnancy is characterized by steady growth IL10 concentrations as found in pregnant control group.

CONCLUSIONS

Thus, pregnancy against HSV-associated HIV infection has a number of clinical and immunological features that distinguish it from both physiological gestation and from HIV-infected patients. First of all it concerns the risk of miscarriage - unlike pregnant women with isolated HIV, patients with HIV-associated GI manifestations are more threats to abortion with vaginal bleeding. An anamnesis datas correlate with immunological – in patients with associated infection revealed a reduced concentration of anti-inflammatory interleukins classes, which is one of the main pathogenetic factors of miscarriage.

Иммунологические изменения у ВИЧ-позитивных беременных с ассоциированной герпетической инфекцией

К.О. Венцковский, А.С. Загородня

В статье представлен анализ клинического течения первой половины беременности у ВИЧ-инфицированных пациенток и у женщин с ассоциированной ВИЧ-ВПГ-инфекцией. Показано, что кроме присущей ВИЧ-инфицированным беременным высокой частоты инфекционных осложнений, исследуемая группа имеет высокий риск невынашивания беременности. Изучены также особенности баланса интерлейкинов у обследованных беременных и их роль в развитии гестационных осложнений.

Ключевые слова: ВИЧ-инфекция, герпетическая инфекция, гестационные осложнения, интерлейкины.

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