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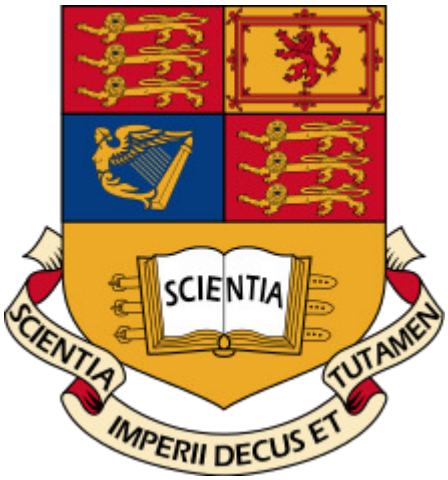

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The study of the diagnostic value of immunoregulatory proteins to assess the functional capacity of the fetoplacental complex with intrauterine infection

Abstract: This article is devoted to the study of the content of immunoregulatory proteins to evaluate the functional capacity of the fetoplacental complex, forecasting and reduce the risk of intrauterine infection (IUI).

Keywords: intrauterine infection, immunoregulatory proteins, placental complex, pro-inflammatory cytokines.

One of the current problems in obstetrics and gynecology are infectious and inflammatory diseases of women during pregnancy [1]. Infection of the urogenital tract of pregnant woman can be realized in the infectious process and manifested pyelonephritis, cystitis, coleitis, chorioamnionitis, fetal infection and the development of intrauterine infection (IUI) [2]. Acute infection may be the cause of pregnancy loss and / or the birth of children with developmental disabilities as a result of direct infection of the fetus and placenta [3,4]. Long persistent, chronic infections often lead to intrauterine infection, can become a cause of placental insufficiency (FPI), which leads to intrauterine growth retardation (IUGR) of the fetus, the defeat of its most important organs of life [5,6]. The share of IUI in the structure of mortality in our country is almost 25%, however, transplacental infection of the fetus is considered to be one of the most probable causes of 80% of congenital malformations, which, in turn, account for about 30% of all deaths of children under 1 year [7].

The immune system of pregnant woman should be adapted to semiallogenny fetus and still be tense with respect to various pathogens of bacterial and viral infections, and changes in the immune system due to viral persistence may result secondary to activation of the bacterial flora and the development of autoimmune disorders and serve the cause of development of a chain of pathological inflammatory reactions [8]. The development of an infectious disease of the newborn affects the evolution of the infection. The spectrum of pathogens causing the intrauterine infection of the fetus and the intrauterine infection of the newborn changed in recent years. There is a growing pathology associated with persistent intracellular so-called slow infection. In general, it is believed that intrauterine infection affects the viability of newborns in 88%. The actual percentage of the negative effects of intrauterine infection is still uncertain. According to various estimates fetal neonatal infection can be observed in every tenth case of pregnancy in the world. However, the true incidence of perinatal pathology caused by an infectious factor, remains unspecified, due to the absence of screening, the cycle of the infection and the incidence of immediate, frequent latent course of the pathological process, the objective complexity of antenatal laboratory diagnostics. As a result, a significant portion of infections remain undiagnosed and statistical analysis is taken into account as a result of complications of childbirth, fetal asphyxia, syndrome of respiratory disorders and other pathological conditions [9]. To detect intrauterine infection apply complex methods, including a variety of diagnostic procedures, but in most cases they reveal either the mere presence of the pathogen in the active or persistent form of the mother or indirect signs of intrauterine infection, that does not mean unavoidable development of an infectious disease of the fetus. The incidence of infection with the manifestation of the disease is on average about 12-14% of all cases of intrauterine infection [10]. Direct antenatal diagnosis of IUI using high-tech invasive techniques (cordocentesis, amniocentesis, chorionic villus or placenta sampling) is rarely used because of the large number of contraindications and possible complications of pregnancy. Diagnostic methods in addition to the clinical and ultrasound include immunoassays of cytokines (IL-1β, TNF-α, IL-8, IL-6, IL-10) which are the predictors of intrauterine infections. Cytokine levels has a great variability, which is not always possible to forecast the development of IUI [11].

Thus the search for reliable methods of antenatal and intrapartum diagnosis of IUI in newborns is still relevant in obstetrics. Thus the development of minimally

invasive techniques allow not only to detect the presence of the pathogen, but also to determine the risk of developing an infectious disease of the fetus and newborn, as well as complications of neonatal period is very important. The mechanisms affecting the fetus has not yet been established. In recent years, there is a popular theory that the damaging effect is not the pathogen, but the synthesis of autoantibodies to the cells of the mother and the fetus, which it provokes. It is believed that such a development of autoimmune processes leads to hyperactivation of the immune system cells and imbalance of the synthesis of proinflammatory cytokines, and as a consequence, there are characteristic for IUI violations. The immunoregulatory proteins modulate cytokine synthesis and there are α -2-macroglobulin (α-2-MG) and lactoferrin (LF). Both proteins are active components of innate immunity, they interact directly with bacterial agents and carry a variety of ions and proteins to cells carrying intercellular interactions, hence changes in the content of these multifunctional proteins help to evaluate the functional capacity of feto-placental complex, as well as to predict the development of the inflammatory response in pregnant [12,13].

The purpose and objectives of the study. Examine the contents of cytokines and immunoregulatory proteins in serum and amniotic waters of the mother, the umbilical cord blood to predict the development of intrauterine infection (IUI).

Materials and methods. Conducted research analysis of the clinical symptoms during pregnancy and its outcomes, the state of the fetus and the newborn in 131 women. All patients were divided into two groups. According to a retrospective analysis of all pregnant women of the main group they was divided into two groups: 1st(n = 58) - with favorable perinatal outcome of labor and the birth of a healthy child (8-9 points Apgar's score); 2nd (n = 40) - with adverse birth outcomes (7 Apgar's score with the implementation of IUI of the different severity and pathological course of the early neonatal period).

The study used clinical, immunological, microbiological, molecular-genetic methods. The analysis of the initial infectious and inflammatory diseases with the determination of the spectrum of possible pathogens. To determine the concentration of α-2-MG in cord blood and serum, and albumin in amniotic fluid using the method of low voltage immunoelectrophoresis. Determination of LF, IL-6, IL-8, TNFα, were determined by enzyme linked immunosorbent assay (ELIZA) using kits "Cytimmune" (USA). The amount of albumin was evaluated using standard biochemical tests. Age

of the patients included in the survey ranged from 22 to 38 years and averaged 34,3 ± 0,5 in the main group and 32,1 ± 0,5 years in the control group.

Results and its discussion. In the study of the structure of infectious and inflammatory diseases, which often leads to perinatal complications found in the study group was significantly more likely to meet a woman who had IgG antibodies to Herpes Simplex Virus 1,2 - 24 patients (24.4%); IgG antibodies to Ch.trachomatis - 19 patients (19.4%); vulvovaginal candidiasis - 16 patients (16.3%); the carrier of Staphylococcus aureus - 8 patients (8.16%); IgG antibodies to CMV - 3 patient (3.06%); mixed carriage of pathogens found in 28 women (28.6%).

In the group of women with various embodiments of the mixed carrier was an increase of LF concentration> 4.9 mg /l and the reduction albumin <37g /l in serum and amniotic fluid was an increase in the level of α-2-MG> 0,08g /l, albumin> 2.4 g /l, Lf level was reduced <5.0 mg /l. High levels of α-2-MG and albumin in amniotic fluid indicates an increase in the permeability of the placental barrier to exposure of proteins from the blood in the amniotic fluid.

The content of LF> 4.1 mg /l increases and decreased albumin <36g /l in serum of the patients with the presence of IgG antibodies to Ch.trachomatis, carriers of Staphylococcus aureus, Candida albicans. The level of LF in the serum of pregnant with IgG antibodies to herpes simplex 1,2 lowers <3.5 mg / l.

The level of α-2-MG > 3.2 g / l and α-1-AT> 4,0g / l was increased in the cord blood of newborns with IUI implementation in carriers of Candida albicans. All infants had reduced the level of LF <2.4 mg / l. The exceptions were the children born of the mothers with IgG to Ch.trachomatis. In our opinion, these results indicate that the products of the inflammatory reaction, the mother get into the fetal circulatory system, increasing the overall anti-proteinase potential of umbilical cord serum as increasing the total concentration of the major proteinase inhibitors - α-MG-2 and α-1-AT.

The amniotic fluid showed a significant increase in the level of α-2 MG > 0.05 mg / l and albumin> 2.4 g / l against decrease LF <4.8 mg / l at the birth of children with IUI, indicating increased permeability of placental barrier and reducing antibacterial and antiviral protection of the fetus.

The greatest change in the level of immunoregulatory proteins have been identified by us in the presence of IgG to Ch.trachomatis, therefore we decided to further explore the concentration of some pro-inflammatory cytokines (IL-6, IL-8, TNFα) in maternal serum, umbilical cord blood and amniotic fluid in the ratio with

protein content. Cytokine content in biological liquids have been studied are subject to considerable individual variability. In the analysis of the results attracted attention a significant increase in the concentration of pro-inflammatory cytokines IL-8 (24358,0 ± 4261,3pg / ml; p = 0.0246) and TNFα (38,6 ± 9,2 pg / ml; p = 0 , 0387), that normally should suppress the synthesis of albumin and α-2-MG, but their levels were also significantly increased. This indicates a serious increase hemato amniotic barrier at IUI and excess of TNFα activates phenomena of apoptosis and synthesis of metalloproteinases, which together with an excess of 2-α-MG can damage tissue, reducing the bactericidal potential of the amniotic fluid. Thus is created a negative inflammatory background, promotes the development of infection of the fetus.

Conclusions. Thus, these data used to determine the level of immu-noregulatory proteins to evaluate the functional capacity of the fetoplacental complex, forecasting and reduce the risk of IUI.

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