The Production and Secretion of IL-10 in the Blood, Depending on the Polymorphism of the IL-10 Gene A-1082G and A-592C in Women with Fetal Growth Retardation

Malyskhina AI1,2, Boyko EL1,*, Sotnikova NYu1,2, Fetisova IN1,2 and Mileeva PL1

1Federal state budgetary institution, Ivanovo Research Institute of Motherhood and Childhood, Ministry of Health of the Russian Federation, Russia
2Federal State Budgetary Educational Institution of Higher Education, “Ivanovo State Medical Academy” of the Ministry of Health of the Russian Federation, Russia

*Corresponding author:
Boyko Yelena Lvovna, Federal state budgetary institution, Ivanovo Research Institute of Motherhood and Childhood, Ministry of Health of the Russian Federation, Ivanovo, Russia

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Introduction
Currently, fetal growth retardation (PFR) remains an urgent problem in modern health care, which is determined by rather high frequency of this pregnancy complication (5-24%) and by the large specific gravity of this pathology in the structure of perinatal morbidity and mortality [1,2]. In the last decade, the hypothesis of “fetal programming” has been discussed in medicine, according to which the health of children can be associated with the conditions of intrauterine development [3]. Most scholars see PFR as a multifactorial disease resulting from the combined action of genetic factors of mother and fetus, as well as environmental factors [4,5]. Part of the risk factors for the development of PFR is associated with a malfunction in the immune system of a pregnant woman. Previously, when studying the cytokine profile of the peripheral blood of pregnant women, a statistically significant decrease in the content of IL-10 in monocytes in women with PFR was revealed compared with the control group [6], however, these changes were mainly associated with exogenous factors.

The purpose of study was to clarify the risk factors for PFR, to analyze the polymorphism of the IL-10 gene and its effect on the production and secretion of this cytokine at a systemic and local level in pregnant women with fetal growth retardation.

Materials and Research Methods
A total of 209 women with a gestational age of 26-39 weeks were examined. The main group consisted of 108 women whose pregnancy was complicated by PFR, which, depending on the degree of PFR, were divided into 2 subgroups: subgroup I - 54 pregnant women with fetometric lagging of fetus from the normative values for this gestational age according to ultrasound data by 2 weeks (PFR of I degree) and II subgroup - 54 patients with a lag of fetometric indicators by 3-4 weeks or more (PFR II-III degree). The control group consisted of 101 pregnant women with no signs of PFR at the time of the examination. Patients taken under supervision were residents of the Ivanovo, Vladimir and Kostroma regions (Central Federal District) and were ethnic Russians. Exclusion criteria: severe preeclampsia, severe extragenital pathology, multiple pregnancy, fetal malformations. Polymorphism of the IL-10 gene A-1082G and A-592C was evaluated by PCR, intracellular production of IL-10 by monocytes by flow cytometry, and the level of IL-10 in supernatants of 24-hour monocyte cultures by ELISA.

Research Results and Discussion
Risk factors for the birth of children with intrauterine growth retardation are: smoking (RR = 1.91), the presence of concomitant extragenital pathology (chronic pyelonephritis (RR = 2.04), thyroid disease (RR = 2.00), abdominal surgery history (RR = 1.95), autonomic dysfunction for hypertonic (RR = 1.86) and hypotonic types (RR = 1.53)), burdened obstetric-gynecological history (uterine fibroids (RR = 2.06), delay fetal growth in previous children (RR = 1.86), habitual miscarriage of early periods, previous medical abortions (RR = 1.75)).

The features of IL-10 A-1082G and A-592C gene polymorphism, which are responsible for the production and secretion of this cytokine, were detected for the first time in pregnant women with fetal growth retardation, who lived in the Central Federal District of Russia. It was revealed that the presence of the IL10 1082A allele in the female genotype in the...
homozygous state is a risk factor for the development of fetal growth retardation of the II-III degree.

In patients with fetal growth retardation of the I degree, in the case of effective therapy, the maximum serum IL-10 content was noted relative to control groups and fetal growth retardation of the II-III degree. In all women with fetal growth retardation during pregnancy, the secretion of IL-10 by monocytes is reduced compared with the control group. In pregnancy with a complicated growth retardation of the II-III degree, intracellular production of IL-10 by monocytes is lower than that of the control group. In all women who gave birth to children with intrauterine growth retardation, the content of IL-10 in the supernatants of 24-hour decidual macrophage cultures in women who gave birth to children with intrauterine growth retardation does not vary from the values of the control group.

For pregnant women with fetal growth retardation of the II-III degree, a significantly more frequent presence in the genotype of the allele IL10-1082A in a homozygous state is characteristic compared with the control group.

In women with fetal growth retardation, regardless of its degree, secretion of IL-10 by monocytes and decidual macrophages is reduced in the presence of a low-functional allele in the genotype IL-10-1082A, while in fetal growth retardation of II-III degree, intracellular production of IL-10 by monocytes is reduced additionally. In women with fetal growth retardation, regardless of degree, the presence of IL-10-592A in the allele genotype is associated with decreased intracellular production of IL-10 by peripheral blood monocytes, and in fetal growth retardation of I degree, macrophages of decidual tissue.

The presence of the IL-10-1082A/G or IL-10-1082A/A genotype in smoking women is a criterion for predicting the development of fetal growth retardation (RR = 3.19) with an accuracy of 85.71%, sensitivity - 91.07% and specificity - 71.43%.

**Conclusion**

The study of the polymorphism of the IL-10 genes of immunocompetent cells in patients with the PFR, including depending on the degree of the PFR, allows us to expand our understanding of the mechanisms of formation of PFR.

**References**