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CHANGES IN THE LEVEL OF FETAL DNA IN BLOOD SERUM OF WOMEN WITH NON-DEVELOPING PREGNANCY

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Based on the study of 257 women with non-developing pregnancies (NDP) of various origin, depending on their underlying cause, we observed different levels of serum fetal DNA. At the same time, in a row sequence of the dynamics of increase of fetal DNA in blood serum of women with NDP of different genesis these indicators were distributed as follows: the 1st place took NDP of associated origin, the 2nd one - NDP of genetic, the 3rd - NDP of hormonal, the 4th - NDP of infectious and the 5th place took NDP of autoimmune origin.

Keywords: Non-developing pregnancy, fetal DNA.

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Introduction

In recent years determination of extracellular DNA is shown to have the predictive and diagnostic significance in modern obstetric practice (Bushtyryova et al., 2007). Interest in the extracellular DNA has increased immeasurably after it became clear that its amount may be increased substantially in a number of diseases that can be recorded as an early sign of relevant pathologies. DNA levels may increase in blood during pregnancy. Gorbachyova et al. (2007) believe that fetal DNA appears in maternal blood already in the first month of pregnancy, and its finding opens new possibilities for noninvasive prenatal diagnosis. A number of researchers (Dimmeler et al., 2000; Huppertz et al., 2005) associate the increase in fetal DNA with the contribution of protein catabolism, excretion of oligonucleotides from the circulation and redistribution in organs and tissues in the mother-placenta-fetus system. According to Zolotukhin (2003), this is normal condition, controlling the process of death of cells and degradation of their chromatin in the body.

The purpose of our research was to assess the level of fetal DNA in the blood of women with non-developing pregnancies, depending on the origin.

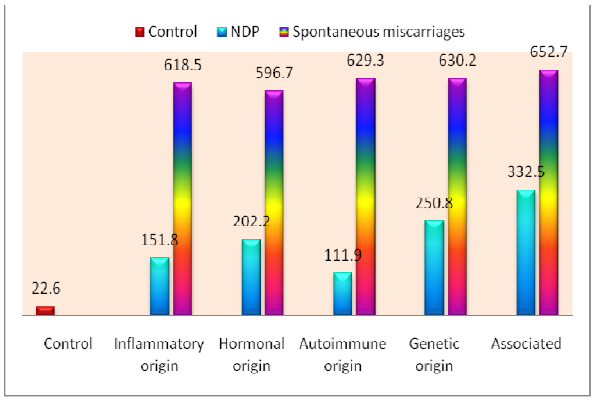
Materials and methods

The study included groups of women with NDP (n=257), in the genesis of which dominated inflammatory diseases of pelvic organs, hormonal, autoimmune disorders, genetic and associated pathologies. Comparison group included women with spontaneous miscarriages (n = 70). Control group consisted of women with physiological pregnancies who had admitted to the hospital for an abortion (n=40). In the main study group fetal DNA levels were determined in blood serum of women in the dynamics of the 1st and 2nd gestation trimesters, whereas in the comparison group - only in the 1st trimester by PCR method on PCR analyzer "Slan" (China) using reagents of "Litex" Ltd. (Russia). The data obtained were processed by the method of variation statistics.

Results and discussion

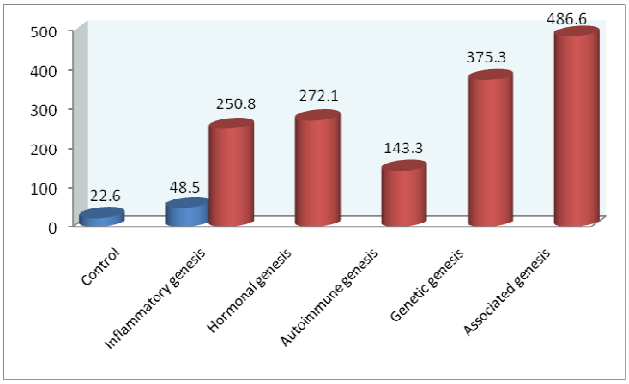
The results have showed that the level of fetal DNA was significantly dependent on risk factor. Thus, the study of the levels of fetal DNA in blood serum of patients in the main group showed that in women with NDP of infectious genesis its content was higher in 6.7 times ($P<0.05$) in the 1st trimester in comparison with the control data. On the contrary, at this gestational age, it was revealed to be lower in 4.1 times, relatively to comparison group ($P<0.001$).

FIGURE 1. DYNAMICS OF FETAL DNA IN GROUPS OF PREGNANT WOMEN IN THE 1ST GESTATION TRIMESTER, DEPENDING ON THE ORIGIN OF NDP (PG/ML)



Similar results we obtained in the analysis of fetal DNA levels when comparing the data of patients with NDP of hormonal origin, respectively to control and comparison groups. A similar trend was also observed in NDP of autoimmune, genetic and associated genesis (Figure 1). Thus, compared with control, in patients with NDP of hormonal, autoimmune, genetic and associated genesis the levels of fetal DNA exceeded in 8.9; 4.9; 11.1 and 14.7 times, respectively ($P<0.001$), whereas compared with such data in the group with spontaneous miscarriages, its levels were lower in 2.9; 5.6; 2.5 and 1.9 times, respectively ($P<0.001$).

FIGURE 2. DYNAMICS OF FETAL DNA IN BLOOD SERUM OF PREGNANT WOMEN IN THE 2ND TRIMESTER, DEPENDING ON THE GENESIS OF NDP (PG/ML)



In the 2nd gestation trimester, the levels of fetal DNA in the main group of patients have been continued to increase, in comparison with control. In this case, the levels of fetal DNA in blood serum of patients with NDP of infectious genesis were increased in 1.7 times, compared to the 1st trimester, and in patients with NDP of hormonal, autoimmune, genetic and associated genesis in 1.3; 1.3; 1.8 and 1.5 times ($P<0.001$), respectively, whereas compared with control it increased in 5.2; 5.6; 2.9; 7.7 and 10.0 times ($P<0.001$) (Figure 2).

Table shows dynamics of fetal DNA in blood serum of pregnant women in the 1st and 2nd gestation trimesters.

TABLE 1. DYNAMICS OF FETAL DNA IN BLOOD SERUM OF PREGNANT WOMEN, PG/ML (M ± M)

Main group	1st trimester	2nd trimester
Inflammatory genesis	151.8±5.67*Δ	250.8±13.94*Δ
Hormonal genesis	202.1±10.30*Δ	272.1±15.13*Δ•
Autoimmune genesis	111.6±8.98*Δ	143.3±10.77*Δ•
Genetic origin	250.8±13.62*Δ	375.3±12.17*Δ•
Associated genesis	332.0±19.77*Δ	486.6±33.35*Δ•
Comparison group		
Inflammatory genesis	616.5±69.28*	-
Hormonal genesis	596.7±56.09*	-
Autoimmune genesis	629.3±78.67*	-
Genetic origin	630.2±75.71*	-
Associated genesis	652.7±80.31*	-
Control group	22.6±2.29	48.5±3.50•

Notes: * - significant differences to control (P<0.05); Δ - significant differences to comparison group (P<0.05); • - significant differences to the indexes of the 1st trimester (P<0.05).

It should be emphasized that even in the control group there is a clear dynamics of increase of fetal DNA with increasing of gestational age. Thus, in the 2nd trimester the levels of fetal DNA were higher in 2.1 times (P<0.001), compared to the 1st trimester.

Therefore, depending on the cause of NDP observed different levels of serum fetal DNA. At the same time, in a row sequence of the dynamics of increase of fetal DNA in blood serum of women with NDP of different genesis these indicators were distributed as follows: the 1st place took NDP of associated origin, the 2nd one - NDP of genetic, the 3rd - NDP of hormonal, the 4th - NDP of infectious and the 5th place took NDP of autoimmune origin.

Conclusion

The revealed dynamics of fetal DNA suggests the possibility of using it to assess the diagnostic value and extent of the destructive process in the placenta, as well as growth of post-apoptic oligonucleosomic fragments of the genome in the body of pregnant women with risk for NDP development.

Thus, the findings suggest the importance of degradation of DNA in the mother-placenta-fetus system in the pathogenesis of NDP. The differences in changes in the level of serum fetal DNA can be recommended for differential diagnosis, to assess the degree of increasing degradation violations in the mother-placenta-fetus system, and for predicting the NDP development in pregnant women.

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