

We analyzed the case histories of patients diagnosed with external genital endometriosis and adenomyosis, who were treated at a medical infertility center during the period of 2017-2019.

In women with infertility associated with endometriosis, pain was found to occur in 43 patients (61.16%). The dependence of the pain syndrome on menstruation was registered (94% of cases). According to case histories, it was found that 42 women had no pregnancies in the past. They were diagnosed with Infertility I, which constituted 66.6%. According to the results of cytological examination, type II was found to predominate in 28 women (73.6%), which indicated an inflammatory process. According to repeated ultrasound data, internal genital endometriosis was not suspected, so it is not reasonable to rely on ultrasound data as an additional method of research, and this requires the use of new diagnostic methods.

Thus, modern medicine must continue to study in detail the diseases that cause infertility. Scientists should investigate the causes of infertility in order to further prevent and successfully treat them.

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CHANGES OF LEVELS OF MELATONIN, CYTOKINES AND PLACENTAL GROWTH FACTOR IN THE UMBILICAL BLOOD TAKEN FROM WOMEN WITH FETAL GROWTH RESTRICTION

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The aim of the study was to investigate changes in melatonin, cytokines' and placental growth factor's concentrations in umbilical blood in case of presence of pathology of pregnancy and childbirth associated with placental dysfunction, manifested by fetal growth restriction.

Changes in melatonin, cytokines' and placental growth factor's (PIGF) levels in umbilical cord blood were studied in 14 mothers with placental dysfunction (PD), which was realized in the form of intrauterine growth restriction syndrome (IUGR). The diagnosis was set on the basis of ultrasound fetometry at a gestational age of 36 weeks. The control group consisted of 13 women with physiological gestation and labor. Levels of melatonin, placental growth factor and cytokines were monitored in venous umbilical cord blood, which was collected during the third period of labor immediately after birth. After the pulsation of the umbilical cord had stopped, it was cut, and blood from the placental end of the umbilical cord was taken to a Vacutainer vacuum tube.

The results of the study of melatonin's, cytokines and PIGF's levels showed that in umbilical cord blood taken during the third period of childbirth in a woman with placental dysfunction, there was a significant decrease in melatonin concentrations comparing to mothers with physiological pregnancy: 7.50 pg / ml (95% confidence interval for median 3.08 – 13.40 pg / ml) versus 14.60 pg / ml (95% confidence interval for median 9.58 – 23.79 pg / ml, $p = 0.0101$). There were no significant differences between the groups in the levels of pro-inflammatory and anti-inflammatory cytokines in umbilical cord blood. Instead, we found that the concentration of PIGF in umbilical cord blood taken to the mother with PD, which manifested itself in the form of IUGR, was 1.57 times lower comparing to mothers with physiological pregnancy: 99.15 pg / ml (95% confidence interval for the median 84.38 – 153.92 pg / ml, in the control group – 155.30 pg / ml (95% confidence interval for the median 98.78 – 354.21 pg / ml, $p < 0.05$).

Thus, the levels of melatonin in umbilical cord blood taken during the third period of labor from mothers whose pregnancies were complicated by IUGR were significantly lower comparing to mothers whose pregnancies had no complications. Therefore, in the blood of the fetus in the case of placental dysfunction, the level of melatonin is also reduced. The pineal gland of both the fetus and the mother does not compensate for the melatonin deficiency that occurs in case of placental dysfunction. In addition, placental growth factor is likely to decrease in umbilical cord blood, and not only in the venous blood of the mother, as we established. Although no statistically significant changes in the cytokines' concentrations were found (possibly due to the small sample size), we found that in placental dysfunction, melatonin correlates moderately with one of the major

proinflammatory cytokines: IL-1- . This suggests that melatonin acts as a moderator of the inflammatory reaction of placental tissue, which is observed in placental dysfunction.

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**SEARCH FOR NEW APPROACHES TO THE TREATMENT OF PRIMARY
PLACENTAL DYSFUNCTION IN PREGNANT WOMEN WITH A HISTORY OF
HABITUAL MISCARRIAGE**

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The development of new treatments for primary placental dysfunction is an extremely relevant research topic in modern obstetrics, considering the role of this pathology in the structure of perinatal morbidity and mortality.

Placental dysfunction (PD) is a clinical syndrome that is associated with impaired placental function (trophic, transport, endocrine, metabolic), which, in its turn, occurs due to morpho-functional changes in the placental tissue initiated by disorders of uteroplacental endothelial perfusion. Placental dysfunction is the cause of fetal distress (distress), growth retardation, pathological conditions and diseases of the newborn. In 60% of cases, PD leads to the formation of fetal growth retardation syndrome. Perinatal mortality in women who experienced PD is 10.3% among full-term infants and 49% among premature infants.

Primary PD is known to develop in early pregnancy (14-18 weeks) under the influence of genetic, endocrine, infectious and environmental factors. Enzymatic insufficiency of decidual tissue, disturbance of structure and localization of the placenta, and defects of vascularization and disturbance of morphology of a chorion play a great role in development of primary PD. In primary PD more often fetal malformations, chromosomal abnormalities and intrauterine infection are detected.

According to the literature, the frequency of placental dysfunction in habitual miscarriage ranges from 50 to 77%. The World Health Organization treats habitual miscarriage as a "three or more consecutive miscarriages by the 20th week of gestation." ASRM experts believe that habitual miscarriage is the occurrence of two consecutive miscarriages, which in its turn increases the prevalence of pathology among married couples of a reproductive age to 5%.

Risk factors for habitual miscarriage: 1. Genetic factors. 2. Anatomical disorders. 3. Congenital anomalies. 4. Microbiological factors. 5. Endocrine factors. 6. Immunological factors. 7. Blood coagulation disorders.

Considering complicated biological processes underlying habitual miscarriage, as well as the significant heterogeneity of research published on this topic, there is widespread uncertainty concerning the optimal individual diagnosis and treatment of women with this pathological condition. Therefore, to improve the quality of care for women with a history of habitual miscarriage and primary placental dysfunction, it is necessary to find a new sound approach to treatment.

Hresko M.D.

**DIFFERENTIATED APPROACH TO A COMPREHENSIVE EXAMINATION AND
MANAGEMENT OF PATIENTS WITH CLIMACTERIC SYNDROME**

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In Ukraine, the scientists dealing with menopause, try to destroy the dominant point of view of non-intervention in the natural biological process of aging and passive observation involutive processes. Clinicians do not always pay due attention to the effects of estrogen deficiency in menopause remote time, shown the development of metabolic syndrome, increased risk of cardiovascular disease, osteoporosis. Until now there was no consensus on tactics differentiated approach in the indication of hormone replacement therapy (HRT) in view of the existing systemic disorders in women.