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OPTIMIZATION OF METHODS FOR DIAGNOSTIC PLACENTAL DYSFUNCTION IN PREGNANT WOMEN

The aim of the study – to find effective and reliable predictors of early diagnosis of placental dysfunction.

Materials and Methods. To solve the tasks, we conducted a study of 60 pregnant women (the main group) with placental dysfunction. The control group consisted of 30 pregnant women with a physiological course of pregnancy, who gave birth to live full-term children with weight and growth characteristics according to the gestation period. The state of the fetoplacental complex was studied based on the study of the levels of hormones (PAPP-A, B-chorionic gonadotropin (B-hCG), progesterone, placental lactogen), biophysical state of the fetus (BPP). To study the uteroplacental and fetoplacental hemocirculation, blood flow spectra were recorded in the uterine arteries, umbilical arteries, and the basin of the middle cerebral artery (MCA) of the fetus. For each vessel, the pulse index (PI), resistance index (IR) and systole were calculated-diastolic ratio (S/D).

Results and Discussion. Based on the analysis of anamnestic data of pregnant women with placental dysfunction, the factors that indicate the development of the pathology are highlighted. As a result of the conducted research on the search for predictors of early diagnosis of placental dysfunction and evaluation of their effectiveness, it was established that the level of human chorionic gonadotropin decreased by 1.3 times, and progesterone in the blood serum at 10–11 weeks decreased by 1.2 times, compared to control and reduction of placental lactogen. Therefore, such signs of CTG, such as a decrease in the amplitude of oscillations less than 3 bpm, the absence of accelerations, the appearance of decelerations, indicate pronounced signs of fetal hypoxia and require timely treatment and a solution to the issue of childbirth. With Doppler blood flow in the uterine arteries, umbilical arteries and veins, it was found that a characteristic sign of a violation of the blood flow velocity curve in the uterine arteries is a decrease in the diastolic component and the appearance of a dicrotic notch in the early diastole phase.

Conclusions. As a result of the analysis, early predictors of placental dysfunction are a decrease in the level of human chorionic gonadotropin, PAPP-A, progesterone, and placental lactogen. For the diagnosis of utero-placental disorders, it is advisable to conduct a dynamic recording of cardiotocography, ultrasound fetometry and placentometry, and to evaluate dopplerometry in the uterine vessels and umbilical artery. It is the complex of these markers that has a high predictive value and makes it possible not only to predict placental dysfunction, but also to diagnose it in a timely and adequate manner.

Key words: fetus; fetal growth retardation; placental dysfunction; placental hormones.

ОПТИМІЗАЦІЯ МЕТОДІВ ДІАГНОСТИКИ ПЛАЦЕНТАРНОЇ ДИСФУНКЦІЇ У ВАГІТНИХ

Мета дослідження – пошук ефективних і достовірних предикторів ранньої діагностики плацентарної дисфункції.

Матеріали та методи. Для вирішення поставлених завдань ми провели дослідження 60 вагітних (основна група) з плацентарною дисфункцією. Контрольну групу склали 30 вагітних із фізіологічним перебігом вагітності, які народили живих доношених дітей з масо-ростовими характеристиками відповідно гестації. Проведено вивчення стану фетоплацентарного комплексу на основі вивчення рівнів гормонів (PAPP), В-хоріонічний гонадотропін (B-hCG), прогестерону, плацентарного лактогену. Стан внутрішньоутробного плода оцінювали за даними ультразвукового дослідження (УЗД), кардіотокографії (КТГ), біофізичного стану плода (БПП). Для вивчення матково-плацентарної і фетоплацентарної гемоциркуляції реєстрували спектри кровотоку в маткових артеріях, артеріях пуповини, басейні середньомозкової артерії (СМА) плода. Для кожної судини обчислювали пульсовий індекс (ПІ), індекс резистентності (ІР) та систоло-діастолічне співвідношення (S/D).

Результати дослідження та їх обговорення. На основі аналізу анамнестичних даних вагітних із плацентарною дисфункцією, виділені фактори, які вказують на розвиток патології. В результаті проведеного дослідження з пошуку предикторів ранньої діагностики плацентарної дисфункції та оцінки їх ефективності встановлено зниження рівня В-хоріонічного гонадотропіну людини – в 1,3 раза, прогестерону в сироватці крові в 10-11 тижнів знижувався в 1,2 раза, порівняно з контролем та зниження плацентарного лактогену. Отже, такі ознаки КТГ, як зниження амплітуди осциляцій менше 3 уд./хв, відсутність акцелерацій, поява децелерацій, свідчать про виражені ознаки гіпоксії плода та потребують своєчасного лікування та вирішення питання про розродження. При доплерометрії кровотоку в маткових артеріях, артеріях і вені пуповини, встановлено, що характерною ознакою порушення кривої швидкості кровотоку у маткових артеріях є зниження діастолічного компонента і поява дикротичної виїмки у фазу ранньої діастоли.

Висновки. В результаті проведеного аналізу ранніми предикторами плацентарної дисфункції є зниження рівня В-хоріонічного гонадотропіну людини, ПАПП-А, прогестерону та плацентарного лактогену. Доцільно для діагностики матково-плацентарних порушень проводити динамічний запис кардіотокографії, ультразвукову фетометрію та плацентометрію та оцінювати доплерометрію в маткових судинах та артерії пуповини. Саме комплекс цих маркерів має високу предикторну значимість і дає можливість не тільки прогнозувати плацентарну дисфункцію, але своєчасно й адекватно діагностувати.

Ключові слова: плід; затримка росту плода; плацентарна дисфункція; плацентарні гормони.

INTRODUCTION. The problem of placental dysfunction attracts the attention of obstetrician-gynecologists as one that is far from being resolved. According to the literature, a violation of the uteroplacental blood flow, which leads to a violation of the growth and functional state of the fetus in the antenatal period, is the cause of a decrease in the adaptation of the newborn in the neonatal period, causes a high morbidity with a violation of the neuropsychological development of the child. Fetal growth retardation is a common complication of pregnancy that is associated with a variety of adverse perinatal outcomes. These are the problem of diagnostic criteria for fetal growth retardation, uncertainty regarding optimal management and delivery time for a fetus with placental dysfunction [1, 2, 3].

Placental dysfunction continues to be the main cause of stillbirth and a cause of obstetric complications. An important point of placental dysfunction is multifactorial pathogenesis. In the development of both early and late onset fetal growth retardation, a special role belongs to placental pathology. Modern literary data indicate new approaches to effective screening of fetal growth retardation based on a comprehensive review: etiology, diagnosis, prenatal monitoring and treatment. Recent advances in new imaging techniques provide the basis for stepwise multiparametric testing that can provide cost-effective screening within existing prenatal care systems [4, 5].

Delay in fetal development is difficult due to difficulties in establishing the causes of this pathology, making a final diagnosis and planning treatment. Fetal retardation is associated not only with a marked increase in the risk of perinatal mortality and morbidity, but also with long-term risks of sequelae. Placental dysfunction is the main factor contributing to the delay in fetal development. Placenta-mediated fetal growth restriction results from chronic fetal hypoxia due to poor placental perfusion through a variety of mechanisms. Visualization of the placenta and uterine artery Doppler, used in conjunction with angiogenic growth factors (in particular, placental growth factor), play an increasingly important role [5, 6].

Previous research suggests that several serious diseases in adulthood, such as coronary heart disease, hypertension, and type 2 diabetes, are associated with fetal growth retardation. These associations were not associated with length of pregnancy, suggesting that they are associated with fetal growth retardation rather than preterm birth. Traditionally, the causes of fetal development delay are divided into fetal, placental, and maternal [7, 8, 9]. Although fetal size is a physical parameter that can be measured at any stage of pregnancy, growth is a dynamic process that can only be assessed by repeated measurements. Therefore, accurate prenatal differentiation between FGR and SGA is difficult. Classification of the severity of fetal growth retardation during pregnancy was proposed on the basis of cardiotocography and Doppler velocity of the umbilical artery (pulsation index) [10,11]. Prenatal diagnosis in the early stages of pregnancy is important for determining the term of pregnancy. Follow-up evaluations are needed to determine whether there is a reduction in fetal growth rate. Several methods are used to detect the condition of the intrauterine fetus, including the height of the uterine fundus (gravigram), ultrasound biometry with fetal weight assessment, and ultrasound Doppler examination [12, 13]. The biometric parameters most commonly used to assess fetal size are biparietal diameter, head circumference, abdominal circumference, and femur length. Using commercially available software integrated into the ultrasound system, fetal weight can be estimated by combining these parameters into a formula. [14].

Placental dysfunction is an important cause of intrauterine, perinatal and neonatal morbidity and mortality [15, 16]. Newborns with delayed fetal development are programmed for metabolic syndrome, cardiovascular diseases, neurodevelopmental disorders, and endocrine anomalies in the long term [17].

MATERIALS AND METHODS. A study was conducted of 60 pregnant women (main group) with placental dysfunction who were being treated at the Ternopil Communal City Hospital No. 2. The control group consisted of 30 pregnant women with a physiological course of pregnancy, who gave birth to live full-term children with weight and growth characteristics in accordance with gestational age.

To assess the functional state of the placenta and fetus, the levels of hormones (PAPP), B-chorionic gonadotropin (B-hCG), progesterone, estriol, and placental lactogen were studied in the first and second trimester. Determination of the hormones of the functional state of the placenta and the fetus was carried out by the method of enzyme-linked immunosorbent assay.

The state of the fetus in utero was evaluated according to ultrasound examination, cardiotocography, determination of the biophysical profile of the fetus. Ultrasound examination of a pregnant woman, determination of biophysical profile was carried out on a Voluson-730 device. Doppler measurements were carried out on the Voluson-730 device with convex sensors with a frequency of 2 to 5 MHz, in color Doppler modes. To study the uteroplacental and fetoplacental hemocirculation, blood flow spectra were recorded in the uterine arteries, umbilical cord arteries, and the pool of the middle cerebral artery (MCA) of the fetus. For each vessel, the pulse index (PI), resistance index (IR) and systolic-diastolic ratio (S/D) were calculated.

Cardiotocograms were recorded using a Cadence basic maternal and child monitoring monitor and a Qiston bT-350 LCD fetal monitor and were evaluated according to the scale of W. Fisher and co-authors (1976).

Statistical processing of the obtained results was carried out on a personal computer with the help of Microsoft Excel office programs using basic statistical methods of calculation. The reliability of the difference between the mean values was determined by calculating the Student's test.

Results and Discussion. Based on the analysis of the anamnestic data of pregnant women with placental dysfunction, we have identified factors that indicate the development of the pathology: extragenital diseases, burdensome gynecological history, placental dysfunction in previous pregnancies. Important criteria for the early diagnosis of placental dysfunction are the transferred Covid during this pregnancy in the first trimester, the threat of termination in the early stages of pregnancy, pregnancy that occurred with the help of assisted reproductive technologies. The age of pregnant women was (25.3±0.2) years in the main group and in the control group (25.6±0.1) years ($P<0.05$).

Analyzing the hormonal state of the mother-placenta-fetus system, we found that with placental dysfunction, the content of B-hCG decreased by 1.3 times, and progesterone

in blood serum decreased by 1.2 times at 10–11 weeks, compared to control (Table 1). The level of estriol was relatively higher in the group with placental dysfunction compared to the control.

Progesterone, which is a protector of pregnancy, plays the main role in the physiological course and prolongation of pregnancy. The data we obtained indicate a relative deficiency of this hormone, which plays one of the leading roles in the process of extending pregnancy and giving birth to a mature newborn. Therefore, it should be considered that the decrease in progesterone level is one of the early diagnostic predictors of placental dysfunction.

Placental lactogen is a specific marker of placental dysfunction because it is of purely placental origin. The placenta synthesizes placental lactogen, which is necessary for the regulation of exchange processes between the body of the mother and the fetus. Analyzing the obtained data, the level of placental lactogen in the examined group was (2.75±0.02) mg/l, and in the control group – (3.78±0.02) mg/l. (Table 2). Consequently, a decrease in the level of placental lactogen in pregnant women with placental dysfunction causes a pathological condition in which the supply of nutrients and oxygen to the fetus is disrupted. And that is why pregnant women of the main group have an inherent depletion of the compensatory and adaptive capabilities of the placenta, which are manifested by a syndrome of fetal growth retardation. A decrease in the level of placental lactogen indicates placental insufficiency and severe fetal condition disorders.

When evaluating the cardiotocogram, depending on the degree of disturbances in the fetoplacental complex, the number of accelerations in 30 minutes of observation decreased, amounting to (1.12±0.03) in the main group, while the indicator was (5.91±0.11) in the control group.

In order to diagnose the intrauterine condition of the fetus in pregnant women with placental dysfunction, criteria were identified that indicate initial signs of fetal distress: a decrease in the number of accelerations to 3, a decrease in the amplitude of oscillations below 5 bpm, the appearance of spontaneous decelerations. Therefore, such signs as a decrease in the amplitude of oscillations less than 3 bpm, the absence of accelerations, the appearance of decelerations, indicate pronounced signs of hypoxia of the fetus and require timely treatment and resolution of the issue of childbirth.

One of the important directions of using ultrasound diagnostics in the evaluation of the fetoplacental system in case of placental dysfunction is placentography, which allows you to determine the localization, size, structure and presence of pathological changes in the placenta. During the study of the localization of the placenta in 60 pregnant women with placental dysfunction, it was found that the placenta is located on the front wall of the uterus almost twice as often (48.3 %) as on the back (26.7 %). 28.0 % and 40.0 % respectively in the control group.

It was found that the indicator of placenta thickness in 12 (20.0 %) pregnant women with placental dysfunction was lower than the standard, and in 8 (13.3 %) – higher than the standard. When studying the echostructure of the placenta in 56.6 % of cases, premature maturation occurred, which occurred in all cases of fetal growth retardation and correlated with the severity of placental dysfunction. An important marker for diagnosing fetal growth retardation in pregnant women with placental dysfunction is a decrease in the amount of amniotic fluid – by 26.7 %.

When comparing the ultrasound results obtained in the second trimester of pregnancy, it was found that only in 12 (20 %) observations were sonographic signs of functional disorders, a change in the volume of amniotic fluid in 6 (10 %) and delayed fetal development – in 8 (13.3) % of observations, which allows us to assert the preservation of adaptive and compensatory features of the fetoplacental complex. In the dynamics of pregnancy in the period of 32–34 weeks, an increase in the share of structural changes of the placenta was established – by 3.2 times, the difference in the volume of amniotic fluid – by 2.6 times, and delays in the development of the fetus – by 1.8 times (14 (23.3 %).

When evaluating the characteristics of blood flow in the uterine arteries, arteries and veins of the umbilical cord, it was established that a characteristic feature in the Doppler study of the violation of the blood flow velocity curve in the uterine arteries is a decrease in the diastolic component and the appearance of a dicrotic notch in the early diastole phase.

When assessing the blood flow in the umbilical cord arteries, it was found that the systolic-diastolic ratio in the main group was (2.85±0.18) and in the control group (2.42±0.15), the same dynamics were observed when assessing PI and IR (Table .3). Pathological increase in the indices of vascular resistance in the umbilical cord artery (Table 3), as it is found in most cases, should be considered as a rearrangement of fetal-placental circulation in order to maintain adequate blood circulation.

Table 1. **The level of hormones of the fetoplacental complex in the first trimester of pregnancy (M±m)**

Indicator	Control group (n=30)	Main group (n=60)
B-chorionic gonadotropin, mmol/ml	40.71±0.68	31.22±0.45*
PAPP-A mmol/ml	2.72±0.01	1.31±0.02*
Progesterone ng/ml	42.71±0.29	35.78±0.68*

Note. *- p<0.05 reliability in comparison with the control group

Table 2. **The level of hormones of the fetoplacental complex in the second trimester of pregnancy (M±m)**

Indicator	Control group (n=30)	Main group (n=60)
Placental lactogen, mg/l	3.78±0,02	2.75±0,02*

Note. *- p<0.05 reliability in comparison with the control group

Table 3. **Indicators of blood flow in the umbilical artery in the third trimester of pregnancy (M±m)**

Indicator	Main group (n=60)	Control group (n=30)
S/D	2.85±0.18*	2.42±0.15
PI	0.96±0.02*	0.83±0.02
IR	0.74±0.03*	0.62±0.04

Note. *- p<0.05 reliability in comparison with the control group

Ultrasound markers of placental dysfunction should be considered premature ripening of the placenta, a decrease in the amniotic index, with dopplerometry a pathological increase in vascular resistance indices in the umbilical cord artery.

CONCLUSIONS. 1. As a result of the analysis, early predictors of placental dysfunction are a decrease in the level of human chorionic gonadotropin, PAPP-A, progesterone, and placental lactogen.

2. For the diagnosis of utero-placental disorders, it is advisable to conduct dynamic recording of cardiotocography, ultrasound fetometry and placentometry, and to evaluate dopplerometry in uterine vessels and umbilical cord arteries. It is the complex of these markers that has a high predictive value and makes it possible not only to predict placental dysfunction, but also to diagnose it in a timely and adequate manner.

PROSPECTS FOR FURTHER RESEARCH. Continue research on the evaluation of the effectiveness of early markers for the diagnosis and treatment of placental dysfunction.

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