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Features of hemodynamics of the mother–placenta–fetus system in the first half of pregnancy after the assisted reproductive technologies application

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Doppler study is one of the main methods for assessing the condition of placental blood circulation and fetal hemodynamics. Doppler blood flow in the uterine arteries demonstrates the broad capabilities of the method for predicting pregnancy complications such as gestosis, fetal development delay, preterm birth, as well as for diagnosing adverse perinatal consequences.
However, there is still no clear opinion about the feasibility of using Doppler as a screening test, as well as about the optimal pregnancy period for this type of study.
The objective: **is to study the hemodynamic features in pregnant women after assisted reproductive technologies (ART) application in the dynamics of the first part of pregnancy.**
Materials and methods**. 299 pregnant women were examined – the main group included 249 women whose pregnancy occurred as a result of ART application. The control group consisted of 50 pregnant women with spontaneous pregnancy and its physiological course. I group – 94 women with tubal-peritoneal factor of infertility, II group – 87 women with endocrine factor of infertility, III group - 68 women whose infertility was caused by the male factor. Doppler ultrasound examination of the uterine arteries, arteries of the umbilical cord and middle cerebral arteries of the fetus were conducted.**
Results**. It was found that the highest intensity of hemodynamics in the uterine artery basin at 11–12 weeks of gestation was recorded in a group of patients with a physiological course of pregnancy. The systolic-diastolic ratio in the right and left uterine arteries in these patients was 1.9 (1.8–2.7) and 2.1 (1.9–2.6), respectively.**
In contrast to women in the control group, pregnant women after ART application analyzed indicators were higher (1.6–1.9 times; p<0.0001). The systolic-diastolic ratio in the right uterine artery in III group was 3.0 (2.4–3.5), I group – 3.3 (3.1–3.4). Similar data were obtained analyzing the curves of blood flow rates in the left uterine artery – 2.9 (2.1–3.5) and 3.0 (2.7–3.6), respectively. The highest peripheral resistance, both in the right (3,6 (3,4–3,7) and left (3,5 (3,2–3,8) uterine arteries, was naturally registered in pregnant women of II group. In 36 (72%) patients with uncomplicated course and successful gestation at 11–12 weeks of pregnancy, blood flow was not recorded in the intervellon space. In the vast majority – 50 (73.5%) pregnant women of I group, two types of blood flow were registered in the intervellar space: pulsating arterial and continuous venous. Only in 18 (26.5%) patients of this group the blood flow in intervellon space was not determined.
As a result of the obtained data analysis, it was found that at 16-17 weeks of gestation, the highest intensity of blood flow in the uterine artery pool was recorded in the control group. Thus, the systolic-diastolic ratio of the right and left uterine arteries in these subjects was 1.6 (1.5–1.8) and 1.8 (1.6–2.0). In pregnant women of the main group, the indicators were significantly higher (1.2-2.0 times; p<0.0001). The systolic-diastolic ratio in the uterine arteries in group III was 2,1 (1,9–2,6); 2,2 (1,9–2,5), in the II group – 3,1 (2,5–3,3); 2,2 (1,9–2,5), in the I group – 2,6 (2,5–3,2); 2,7 (2,5–2,9).
In contrast to the control group, in which the systolic-diastolic ratio in the fetal umbilical artery was 3.4 (3.3–3.5), in III group patients, there was a significantly higher intensity of umbilical blood flow (S/D – 3.3 (3.5–3.6), p=0.03). At the same time, feto-placental hemodynamics in II and I groups patients was characterized by a significant increase in the numerical values of blood flow in the umbilical arteries (S/D – 4.5 (4.4–4.7), p=0.0001 and 3.5 (3.5–3.6), p=0.03, respectively). In patients of the control group, the systolic-diastolic ratio of the middle cerebral artery of the fetus at 16–17 weeks of gestation was 3.4 (3.4–3.5), almost completely coinciding with the same indicator in the umbilical artery (S/D – 3.4 (3.3–3.5).
Patients of group III had a higher blood flow intensity, as evidenced by significantly lower (S/D 3.2 (3.1–3.3), compared with the control group (S/D 3.4 (3.4–3.5) absolute values of the systolic-diastolic ratio. An increase in the intensity of blood flow in the fetal medial artery (against the background of increased vascular resistance in the umbilical artery) was also recorded in the group of subjects of group II (S/D – 2.8 (2.7–2.9). High absolute values of systolic-diastolic ratio in the indicated vessel (4.4 (4.3–4.5) were found in the fetuses of the examined group and group, which characterize a significant decrease in the intensity of cerebral blood flow, compared with all the analyzed groups.
Conclusions**. Thus, the results of the study allow us to attribute Doppler ultrasound to highly informative research methods that make it possible to predict hemodynamic changes in the mother-placenta-fetus system, depending on the type of infertility, take preventive measures and start correction in time.**
Keywords: *pregnancy, assisted reproductive technologies, Doppler ultrasound, uterine arteries, systolic-diastolic ratio.*

Особливості гемодинаміки системи мати–плацента–плід у першій половині вагітності після застосування допоміжних репродуктивних технологій

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Одним з основних методів оцінювання стану плацентарного кровообігу й гемодинаміки плода є допплерометричне дослідження. Допплерометрія кровотоку у маткових артеріях демонструє широкі можливості методу для прогнозування таких ускладнень вагітності, як гестоз, затримка розвитку плода, передчасні пологи, а також для діагностики несприятливих перинатальних наслідків. Однак сьогодні немає однозначної думки як про доцільність використання допплерометрії у якості скринінгового тесту, так і про терміни вагітності, оптимальні для даного виду дослідження.
Мета дослідження: вивчення у динаміці першої половини вагітності особливостей гемодинаміки у вагітних після застосування допоміжних репродуктивних технологій (ДРТ).
Матеріали та методи. Обстежено 299 вагітних. До основної групи увійшли 249 жінок, вагітність яких настала у результаті застосування ДРТ: I група – 94 жінки з трубно-перитонеальним фактором безплідності, II група – 87 жінок з ендокринним фактором безплідності, III група – 68 жінок, безплідність яких зумовлена чоловічим фактором. Вагітним проведено допплерометричне визначення показників маткових артерій, артерій пуповини та середньомозкових артерій плода. До контрольної групи увійшли 50 жінок зі спонтанним настанням вагітності та її фізіологічним перебігом.

Результати. Установлено, що найбільш високу інтенсивність гемодинаміки у басейні маткових артерій в 11–12 тиж гестації реєстрували у групі пацієнток із фізіологічним перебігом вагітності. Показники систоло-діастолічного співвідношення у правій і лівій маткових артеріях у цих пацієнток становили 1,9 (1,8–2,7) і 2,1 (1,9–2,6) відповідно.
На відміну від жінок контрольної групи, у вагітних після використання ДРТ проаналізовані показники були вищими (в 1,6–1,9 разу; p<0,0001). Систоло-діастолічне співвідношення у правій матковій артерії у III групі становило 3,0 (2,4–3,5), у I групі – 3,3 (3,1–3,4). Аналогічні дані були отримані під час аналізу кривих швидкостей кровотоку у лівій матковій артерії – 2,9 (2,1–3,5) і 3,0 (2,7–3,6) відповідно. Найбільш високий периферійний опір як у правій (3,6 (3,4–3,7), так і в лівій (3,5 (3,2–3,8) маткових артеріях закономірно реєстрували у вагітних II групи.
У 36 (72%) пацієнток з неускладненим перебігом і успішним результатом гестації в 11–12 тиж вагітності в інтервельозному просторі кровотік не реєстрували. У переважної більшості – 50 (73,5%) – вагітних I групи фіксували два типи кровотоку у міжворсинчастому просторі: пульсівний артеріоподібний і безперервний венозноподібний. Лише у 18 (26,5%) пацієнток цієї групи кровотік в інтервельозному просторі не визначали.
У результаті аналізу отриманих даних встановлено, що у 16–17 тиж гестації найбільш високу інтенсивність кровотоку у басейні маткових артерій реєстрували у контрольній групі. Так, показники систоло-діастолічного співвідношення правої й лівої маткових артерій у цих обстежуваних становили 1,6 (1,5–1,8) і 1,8 (1,6–2,0). У вагітних основної групи показники були вірогідно вищі (в 1,2–2,0 разу; p<0,0001). Систоло-діастолічне співвідношення у маткових артеріях у III групі становило 2,1 (1,9–2,6); 2,2 (1,9–2,5), у II групі – 3,1 (2,5–3,3); 2,2 (1,9–2,5), у I групі – 2,6 (2,5–3,2); 2,7 (2,5–2,9).
На відміну від обстежуваних контрольної групи, у яких систоло-діастолічне співвідношення в артеріях пуповини плода становило 3,4 (3,3–3,5), у пацієнток III групи відзначали вірогідно більш високу інтенсивність пуповинного кровотоку (S/D – 3,3 (3,5–3,6); p=0,03). У той самий час, фетоплацентарна гемодинаміка у пацієнток II і I груп характеризувалась достовірним збільшенням чисельних значень показників кровотоку в артеріях пуповини (S/D – 4,5 (4,4–4,7); p=0,0001 і 3,5 (3,5–3,6); p=0,03 відповідно). У пацієнток контрольної групи систоло-діастолічне співвідношення у середній мозковій артерії плода у 16–17 тиж гестації становило 3,4 (3,4–3,5), практично повністю збігаючись із аналогічним показником в артерії пуповини (S/D – 3,4 (3,3–3,5).
У пацієнток III групи відзначена вища інтенсивність кровотоку, про що свідчили вірогідно нижчі (S/D 3,2 (3,1–3,3) порівняно з контрольною групою (S/D 3,4 (3,4–3,5) абсолютні значення систоло-діастолічного співвідношення. Підвищення інтенсивності кровотоку у середньомозковій артерії плода (на тлі підвищення судинного опору в артерії пуповини) реєстрували й в обстежуваних II групи (S/D – 2,8 (2,7–2,9).
У плодів обстежених з I групи виявлені найвищі абсолютні значення систоло-діастолічного співвідношення у зазначеній судині – 4,4 (4,3–4,5), що характеризують істотне зниження інтенсивності церебрального кровотоку порівняно з усіма аналізованими групами.
Заключення. Отже, результати дослідження дозволяють віднести допплерометрію до високоінформативних методів дослідження, що дають можливість передбачити гемодинамічні зміни системи мати–плацента–плід залежно від виду безплідності, провести профілактичні заходи та вчасно розпочати корекцію.
Ключові слова*: вагітність, допоміжні репродуктивні технології, допплерометрія, маткові артерії, систоло-діастолічне співвідношення.*

Особенности гемодинамики системы мать–плацента–плод в первой половине беременности после применения вспомогательных репродуктивных технологий

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Одним из основных методов оценки состояния плацентарного кровообращения и гемодинамики плода является допплерометрическое исследование. Допплерометрия кровотока в маточных артериях демонстрирует широкие возможности метода для прогнозирования таких осложнений беременности, как гестоз, задержка развития плода, преждевременные роды, а также для диагностики неблагоприятных перинатальных последствий. Однако до сих пор нет однозначного мнения как о целесообразности использования допплерометрии в качестве скринингового теста, так и о сроках беременности, оптимальных для данного вида исследования.
Цель исследования: изучение в динамике первой половины беременности особенностей гемодинамики у беременных после применения вспомогательных репродуктивных технологий (ВРТ).
Материалы и методы. Обследовано 299 беременных. В основную группу вошли 249 женщин, беременность которых наступила в результате применения ВРТ: I группа – 94 женщины с трубно-перитонеальным фактором бесплодия, II группа – 87 женщин с эндокринным фактором бесплодия, III группа – 68 женщин, бесплодие которых обусловлено мужским фактором. Беременным проведено допплерометрическое определение показателей маточных артерий, артерий пуповины и среднемозговых артерий плода. В контрольную группу вошли 50 беременных со спонтанным наступлением беременности и ее физиологическим течением.
Результаты. Установлено, что наиболее высокая интенсивность гемодинамики в бассейне маточных артерий в 11–12 нед гестации регистрировали в группе пациенток с физиологическим течением беременности. Показатели систоло-диастолического соотношения в правой и левой маточных артериях у этих пациенток составили 1,9 (1,8–2,7) и 2,1 (1,9–2,6) соответственно.
В отличие от женщин контрольной группы, у беременных после использования ВРТ проанализированные показатели были выше (в 1,6–1,9 раза; p<0,0001). Систоло-диастолическое соотношение в правой маточной артерии в III группе составило 3,0 (2,4–3,5), в I группе – 3,3 (3,1–3,4). Аналогичные данные были получены при анализе кривых скоростей кровотока в левой маточной артерии – 2,9 (2,1–3,5) и 3,0 (2,7–3,6) соответственно. Наиболее высокое периферическое сопротивление как в правой (3,6 (3,4–3,7), так и в левой (3,5 (3,2–3,8) маточных артериях закономерно регистрировали у беременных II группы.
У 36 (72%) пациенток с неосложненным течением и успешным результатом гестации в 11–12 нед беременности в интервеллезном пространстве кровоток не регистрировали. У подавляющего большинства – 50 (73,5%) – беременных I группы фиксировали два типа кровотока в межворсинчатом пространстве: пульсирующий артериоподобный и непрерывный венозноподобный. У 18 (26,5%) пациенток этой группы кровоток в интервеллезном пространстве не определяли.
В результате анализа полученных данных установлено, что в 16–17 нед гестации наиболее высокую интенсивность кровотока в бассейне маточных артерий регистрировали в контрольной группе. Так, показатели систоло-диастолического соотношения правой и левой маточных артерий у этих обследуемых составили 1,6 (1,5–1,8) и 1,8 (1,6–2,0) соответственно. У беременных основной группы показатели были достоверно выше (в 1,2–2,0 раза; p<0,0001). Систоло-диастолическое соотношение в маточных артериях в III группе составило 2,1 (1,9–2,6); 2,2 (1,9–2,5), во II группе – 3,1 (2,5–3,3); 2,2 (1,9–2,5), в I группе – 2,6 (2,5–3,2); 2,7 (2,5–2,9).
В отличие от обследуемых контрольной группы, у которых систоло-диастолическое соотношение в артерии пуповины плода составило 3,4 (3,3–3,5), у пациенток III группы отмечали достоверно более высокую интенсивность пуповинного кровотока (S/D – 3,3 (3,5–3,6); p=0,03). В то же время фетоплацентарная гемодинамика у пациенток II и I групп характеризовалась достоверным увеличением численных значений показателей кровотока в артериях пуповины (S/D – 4,5 (4,4–4,7); p=0,0001 и 3,5 (3,5–3,6); p=0,03 соответственно). У пациенток контрольной группы систоло-диастолическое соотношение в средней мозговой артерии плода в 16–17 нед гестации составило 3,4 (3,4–3,5), практически полностью совпадая с аналогичным показателем в артерии пуповины (S/D – 3,4 (3,3–3,5).
У пациенток III группы отмечена более высокая интенсивность кровотока, о чем свидетельствовали достоверно более низкие (S/D – 3,2 (3,1–3,3) по сравнению с контрольной группой (S/D – 3,4 (3,4–3,5) абсолютные значения систоло-диастолического соотношения. Повышение интенсивности кровотока в среднемозговой артерии плода (на фоне повышения сосудистого сопротивления в артерии пуповины) регистрировали и у обследуемых II группы (S/D – 2,8 (2,7–2,9).

У плодов обследованных из I группы выявлены высокие абсолютные значения систоло-диастолического соотношения в указанном сосуде – 4,4 (4,3–4,5), что характеризуют существенное снижение интенсивности церебрального кровотока по сравнению со всеми анализируемыми группами.

Заключение. Таким образом, результаты исследования позволяют отнести допплерометрию к высокоинформативным методам исследования, предоставляющих возможность предсказать гемодинамические изменения системы мать–плацента–плод в зависимости от вида бесплодия, провести профилактические меры и вовремя начать коррекцию.

Ключевые слова: *беременность, вспомогательные репродуктивные технологии, допплерометрия, маточные артерии, систоло-диастолическое соотношение.*

As of this date, a Doppler ultrasound is the main method for assessment of placental circulation and fetal hemodynamics [1, 2].

The powerful capabilities of this method to predict such complications of pregnancy like preeclampsia, delayed fetal growth, premature birth and adverse perinatal consequences, are demonstrated in most studies on Doppler blood flow measurement in uterine arteries [2, 5, 6]. However, there is still no consensus on whether to use Doppler as a screening test or just for pregnancy term determination [3]. In addition, there is no unified judgment on the criteria that characterize the pathological type of blood flow velocity curves in early pregnancy [3, 5].

The mechanism that ensures the constancy of uteroplacental blood flow during pregnancy progression is based on a decrease in placental resistance to blood flow. During the pregnancy term, about 100 spiral arteries connect the maternal blood circulation with the placental vascular pool that forms the intervillar space. These vessels undergo important physiological changes that are necessary for a 10-fold increase in blood circulation, providing the metabolic needs of the placentofetal complex [2, 4]. During the first trimester of gestation, the first wave of endovascular trophoblast invasion in the walls of the decidual spiral arteries occurs and ends at the level of junction of the decidua basalis and myometrium at 15 weeks of pregnancy. During the second trimester of pregnancy, a second wave of trophoblast invasion in the muscle layer of the spiral arteries before interacting with the end sections of the radial arteries occurs. During this process the muscle-elastic elements of spiral artery walls are replaced with a mixture of fibrinoid and connective tissue that forms fibrinoid wall necrosis. As a result of this unique process, the shell of the spiral arteries is completely devoid of non-striated muscle elements and becomes insensitive to the action of various hypertensors. This replacement of small spiral arteries with larger vascular channels will transform the uteroplacental blood circulation from a highly resistant to a low-resistant vascular system. The described changes are a necessary feature of the physiological development of pregnancy [2, 5]. Violation in the processes of trophoblast invasion leads to high blood flow resistance in the uteroplacental system and pathogenetically determines the complicated course of gestation [2, 4, 5].

The objective: is to study the hemodynamic features in pregnant women after assisted reproductive technologies (ART) application in the dynamics of the first part of the pregnancy.

MATERIALS AND METHODS

A comparative analysis of blood flow indexes in the uterine arteries in patients whose pregnancy occurred as a result of the ART application and women with a physiological course of pregnancy in the first half of pregnancy was conducted. One of the mandatory rules for studying uteroplacental hemodynamics is to evaluate the curves of blood flow rates in both uterine arteries, which is due to the fact that in the complicated course of gestation, blood flow disorders in most cases appear only in one of the uterine arteries [2].

In the dynamics of the prospective study, 299 pregnant women were comprehensively examined. They were divided as follows: the main group included 249 women whose pregnancy occurred as a result of the ART application, and the control group - 50 pregnant women with spontaneous pregnancy and its physiological course, who were registered for pregnancy in the period of 6-8 weeks.

Women of the main group, who became pregnant as a result of ART application, were divided into three groups, depending on the factor that caused infertility. The I group included 94 women with tubal-peritoneal factor of infertility, the II group was formed by 87 women with endocrine factor of infertility, the III group included 68 women whose infertility is caused by the male factor. Pregnant women in the study groups were representative by age, marital and social status and place of residence, which allowed to judge further about the differences caused by the etiological factors of infertility.

The pregnant women of the examined groups underwent standard clinical and laboratory tests, which included general blood and urine analysis, as well as Doppler ultrasound measurements in the uterine arteries, umbilical cord arteries and middle cerebral arteries of the fetus. The examination was conducted on Toshiba, Xario 100, Ultrasound system in the first part of pregnancy.

RESULTS OF THE RESEARCH AND DISCUSSION

As follows of the analysis of the obtained data, it was found that the highest intensity of hemodynamics in the uterine artery pool at 11–12 weeks of gestation was recorded in the group of patients with a physiological course of pregnancy. Thus, the systolic-diastolic ratio in the right and left uterine arteries in these patients was 1.9 (1.8–2.7) and 2.1 (1.9–2.6) respectively.

The analyzed indicators in pregnant women with ART application were significantly higher (1.6–1.9 times; $p<0.0001$) than in women with uncomplicated course of pregnancy (Control group). The systolic-diastolic ratio in the right uterine artery in the III group was 3.0 (2.4–3.5) and in the I group – 3.3 (3.1–3.4). Similar data were obtained when analyzing the curves of blood flow rates in the left uterine artery-2.9 (2.1–3.5) and 3.0 (2.7–3.6), respectively.

The highest peripheral resistance, both in the right (3,6 (3,4–3,7)) and left (3,5 (3,2–3,8)) uterine arteries, was naturally registered in pregnant women of the II group.

The main morphological substrate of pathological curves of blood flow rates in the uterine arteries is the absence or incomplete invasion of the trophoblast in the spiral arteries, which leads to increased resistance in the uteroplacental pool and, obviously, determines the different nature of changes in the hemodynamics of the intervellon space.

The interstitial space of the placenta in the form of cavities labyrinth was first described by William et John Hunter in the XIX century, but there is still disagreement about the circulation of maternal blood in it.

Author's research allowed establishing that in the vast majority of 36 (72%) patients with uncomplicated course and a favorable gestational outcome at 11–12 weeks of pregnancy the blood flow in the intervellon space was not registered. The continuous venous blood flow during color Doppler mapping was revealed in less than the third part of the patients – 14 (28%). None of the pregnant women in this group didn't have the arteriotony pulsating blood flow. The obtained data allowed to conclude that the physiological course of gestation is most characterized by the lack

of registration of blood flow in the interstitial space in the first trimester of pregnancy.

Comparison of the obtained data with the evaluation of the blood flow velocity curves in the uterine arteries allowed to identify some of them. In the absence of blood flow in the intervellon space, the absolute values of the systolic-diastolic ratio in the right and left uterine arteries were significantly lower – 1.8 (1.7–1.9) and 2.0 (1.8–2.2) respectively, than in cases with venous blood flow-2.6 (2.4–2.9) and 2.9 (2.7–2.9), respectively.

The data obtained are aligned with the views of various researchers on the process of hemocirculation formation in the interstitial space, despite their inconsistency.

For instance, E.C. Kingdom, P. Kaufinann (1999), J. Aplin, (2000) deny the presence of blood flow in the intervellon space in the first trimester of the physiological pregnancy, based on the fact that due to early endovascular invasion, cytotrophoblast cells completely obliterate the lumen of spiral arteries, forming cytotrophoblastic plugs, which are a kind of barrier (cell filter) that prevent the mother's blood from entering the interstitial space.

In contrast, the vast majority – 50 (73.5%) in pregnant women of I group two types of blood flow in the intervertebral space was registered: pulsating arterial and continuous venous. Only in 18 (26.5%) patients of this group the blood flow in intervellon space was not determined. It is necessary to pay attention to the fact that it was in the latter that the intensity of blood flow in the uterine arteries was as close as possible to the indicators of patients with favorable pregnancy outcomes (the values of the systolic-diastolic ratio in the right and left uterine arteries, respectively, were 2.0 (1.9–2.6) and 2.1 (2.1–2.3). It is interesting that these subjects had a late manifestation (31–32 weeks) of fetal growth retardation.

In contrast, the systolic-diastolic ratio in the right and left uterine arteries was significantly higher in patients with a pulsating arterial type of blood flow in the intervellon space – 3.2 (2.9–3.4) and 3.3 (2.7–3.6), respectively. Approximately the same data were obtained recording continuous venous blood flow (systolic-diastolic ratio in the right and left uterine arteries was 3.3 (2.7–3.5) and 3.3 (2.9–3.6), respectively.

The pulsating arterial wave of blood flow velocity curves corresponds to the «fountain» release of blood from the lumen of spiral arteries, in our opinion, indicates incomplete gestational restructuring and preservation of non-striated muscle fibers in the walls of these vessels. However, continuous venous profile of the Doppler signals from blood flow, drains scattered in decidual shell venous holes, obviously, is one of the first mechanisms to compensate for the hemodynamic blood flow in the functional subsystem of the system «mother–placenta–fetus».

Arteriole and venous types of blood flow were registered in the interstitial space of the overwhelming majority (69 (79.3%) of in II group patients, as well as in the I one. In the remaining 18 (20.7%) subjects of this group, there was no blood flow in the intervellon space. In I group of patients, the fundamental difference from the latter was that in all analyzed cases, the absolute values of the systolic-diastolic ratio in the right and left uterine arteries exceeded 3.3, which indicates a high peripheral resistance in the utero-placental pool.

Physiological restriction of the incoming volume and pressure of maternal blood is essential for the normal development of pregnancy. It can be assumed that during the physiological course of gestation, «plugs» of trophoblastic cells in the spiral arteries prevent the mother's blood from entering the interstitial space, protecting the chorion villi from high blood pressure in the uterine artery pool. An increase in blood pressure in the intervellon space, as a result of high peripheral resistance in the uterine vessels, can significantly disrupt the connection of the chorion with the uterine wall and lead to its ischemia and exfoliation.

In our opinion, the state of hemodynamic processes occurring in the intervelous space in III group pregnant women is of extreme interest. The vast majority of patients in this group, 80 (85.1%), had no blood flow in the interstitial space, and only 14 (14.9%) of the examined patients had a pulsating arterioid type of blood flow. In contrast to I group pregnant women, in II group patients, the absence of blood flow in the intervillar space was accompanied by significantly high absolute values of the systolic-diastolic ratio in the right and left uterine arteries – 3.3 (3.2–3.5) and 3.0 (2.8–3.6), respectively.

The mechanisms of regulation of blood flow in the interstitial space are still the subject of research. A. Karimu and G. Burton (1993) believed that blood pressure in the vascular villi network plays a role in regulating both their total volume and location in the interstitial space. With increasing blood pressure in the feto-placental pool (for example, with the development of hypoxia), the total functional surface area of the villi and the distance between them expands, which increases the possibility of gas exchange.

As a result of the obtained data analysis, it was found that, both at 11–12 and 16–17 weeks of gestation, the highest intensity of blood flow in the uterine artery pool was recorded in the group of patients with a physiological course of pregnancy. Thus, the systolic-diastolic ratio of the right and left uterine arteries in these subjects was 1.6 (1.5–1.8) and 1.8 (1.6–2.0), respectively. Our own research confirms the opinion of most authors that the maximum reduction in uterine artery resistance, which is characteristic of pregnancy with a physiological course, occurs exactly before 16 weeks [2, 3]. This means the completion of morphological changes in the spiral arteries and the final formation of low-resistant blood flow in the uterine artery basin.

In pregnant women after ART application, the analyzed indicators were significantly higher (1.2–2.0 times; $p<0.0001$). The systolic-diastolic ratio in the right uterine artery in the III group was 2.1 (1.9–2.6), in the II group – 3.1 (2.5–3.3), in the I group – 2.6 (2.5–3.2). Similar data were obtained during the analysis of the curves of blood flow rates in the left uterine artery (2,2 (1,9–2,5); 3,2 (2,6–3,4); 2,7 (2,5–2,9) respectively). The obtained data illustrate the inferiority of the second wave of trophoblast invasion, which is completed by this gestation period.

In contrast to the control group, in which the systolic-diastolic ratio in the fetal umbilical artery was 3.4 (3.3–3.5), III group patients, despite slight differences in absolute values, had significantly higher intensity of umbilical blood flow (S/D – 3.3 (3.5–3.6); $p=0.03$).

At the same time, feto-placental hemodynamics in patients of I and II groups were characterized by a significant increase of numerical values of indicators of blood flow in the umbilical artery (S/D – 4,5 (4,4–4,7); $p=0.0001$ and 3.5 (3,5–3,6); $p=0.03$, respectively), indicating increased peripheral vascular resistance of fetal part of the placenta, morphological substrate of which is the reduction of vascularization and microvascular lesions of terminal villi.

Certain features were also revealed in the study of blood flow indicators in the fetal midbrain artery. Based on the research of Orlov (2006), first identified and explained the existence of the 5 periods in the prenatal development of the fetus, each of which manifests a certain ratio of Doppler as uterine and fetal vessels [2], the investigated period of gestation (weeks 16–17) identified by the author as the initial stage of starting the physiological hypoxemia, characterized by a low level of oxygen in interstitial space and impressive stability (almost identical to the performance of systolic-diastolic ratio in umbilical artery, aorta and mid-cerebral artery of the fetus) blood flow in the main fetal vessels during the physiological course of gestation. In our study, in control group patients, the systolic-diastolic ratio of the fetal middle cerebral artery at 16–17 weeks of gestation was 3.4 (3.4–3.5), almost completely coinciding with the same indicator in the umbilical artery (S/D – 3.4 (3.3–3.5).

Thus, patients of III group had a higher intensity of blood flow in the indicated vessel, as evidenced by significantly lower (S/D 3.2 (3.1–3.3), compared with control group (S/D 3.4 (3.4–3.5) absolute values of the systolic-diastolic ratio. An increase in the intensity of blood flow in the fetal medial artery (against the background of increased vascular resistance in the umbilical artery) was also recorded in the II group (S/D – 2.8 (2.7–2.9).

The occurrence of early centralization of fetal blood circulation with hyperperfusion of intracranial structures that develop in a situation of utero-placental hemodynamics deficiency is another compensation mechanism in the hemodynamic subsystem of the functional system «mother–placenta–fetus».

On the contrary, the fetuses examined from I group showed higher peripheral resistance in the middle cerebral artery of the fetus (as well as in the umbilical artery). It should be noted that this category of subjects recorded the highest absolute values of the systolic-diastolic ratio in the specified vessel – 4.4 (4.3–4.5), which characterize a significant decrease in the intensity of cerebral blood flow, compared with all the analyzed groups.

The study of hemodynamic features in the fetoplacental complex at 20–22 weeks of gestation also revealed a number of patterns.

Thus, in control group patients, against the background of stable hemodynamic parameters in the uterine arteries (almost identical to similar indicators at 16–17 weeks), there was a further increase in the intensity of blood flow in the umbilical artery (S/D-3.1 (2.6–3.4) and an increase in peripheral vascular resistance in the middle cerebral artery of the fetus (S/D – 4.1 (3.6–4.4).

Special attention deserves the fact that I groups fetuses again as in 16–17 weeks of gestation, the highest absolute values of systolo-diastolic ratio in umbilical artery (3,6 (3,4–3,7) and middle cerebral artery of the fetus (4,6 (4,5–4,8) were observed. Those indicate the absence of a compensatory mechanism which ensures an adequate cerebral hemodynamics.

CONCLUSIONS

Thus, the results of the study allow us to attribute Doppler ultrasound to highly informative research methods that make it possible to predict hemodynamic changes in the mother-placenta-fetus system, depending on the type of infertility, conduct preventive measures and proper correction in time.

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