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THE SIGNIFICANCE OF ANGIOGENIC BIOMARKERS AND HEMOSTATIC SYSTEM PARAMETERS IN FORECASTING PREGNANCY COMPLICATIONS FOLLOWING IVF

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Abstract
The article shows that early detection of disorders in the hemostasis system by the type of genetic thrombophilia and genetically non-deterministic hypercoagulation, as well as timely diagnosis of changes in the levels of angiogenic growth factors (soluble receptor of vascular endothelial growth factor 1and placenta growth factor) in the first trimester of pregnancy allows us to identify risk factors for the development of the threat of termination of pregnancy, PI and gestosis in pregnant women after IVF

Keywords: Pregnancy, genetic thrombophilia, hypercoagulation, angiogenic growth factors

Introduction

Currently, it has been proven that the formation of pregnancy complications is based on violations of the stages of trophoblast invasion and insufficient transformation of spiral arteries, leading to a decrease in blood supply to the growing placenta, hypoxia, impaired secretion of angiogenic factors, spontaneous miscarriages, intrauterine growth retardation and fetal death, placental abruption and gestosis [1,2]. In the pathogenesis of pregnancy complications such as placental insufficiency, fetal growth retardation syndrome, preeclampsia, an important role is played by an imbalance in the production of growth factors

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responsible for both the condition of the vascular wall and angiogenesis of the placenta and, accordingly, for its proper formation and development.
Pathological invasion of the trophoblast into the spiral arteries contributes to the development of various pregnancy complications, leads to placental ischemia and gestosis, placental insufficiency and fetal growth retardation syndrome [3-6]. Chorion detachment and fetal loss in early pregnancy account for 20-25% of all pregnancies [1,7,8].
The pathology of gestational restructuring of the spiral arteries of the placental bed is explained by incomplete or insufficient invasion of the extracellular cytotrophoblast (IEC), the activity of which is regulated by local growth factors. If it is if it occurs during the first wave of invasion, then there is a delay in the onset of uteroplacental circulation, necrotic areas in the endometrium are formed, up to the complete separation of the anchor villi and the placental bed, which leads to the death of the embryo. The insufficiency of the second wave of CT invasion into the myometral segments does not ensure proper expansion of the spiral arteries and an adequate increase in the volume of uteroplacental circulation [9,10]. Increased concentration of soluble vascular endothelial growth factor receptor (sVEGFR-1) and decreased concentration of placental growth factor (PlGF) play a role in the pathogenesis of gestosis and placental insufficiency [11].
Prolonged hormonal preparation of patients for IVF is an additional trigger for the occurrence of thrombophilia complications. Hormonal load leads not only to direct activation of the hemostasis system, but also to secondary hypercoagulation, chronic DIC syndrome, and proinflammatory status [12-15].
The identification of markers of thrombophilia, key markers of angiogenesis, will allow us to develop modern approaches to the diagnosis of pregnancy complications after IVF at the preclinical stage of their development and to carry out early prevention and therapy.

The aim of the study was to identify the relationship between disorders of hemostasis, angiogenic growth factors and pregnancy complications after IVF.
A prospective study of 53 patients with tubal-peritoneal and male infertility factors entering the ART program was conducted. Depending on the data

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obtained, they were divided by us into 3 groups. The main group consisted of 18 patients with established thrombophilia, including multifactorial forms. The comparison group consisted of 21 patients without thrombophilia, but with a violation of the hemostasis system in the form of severe hypercoagulation, significantly different from hypercoagulation in physiological pregnancy, the so-called chronic form of DIC syndrome on the background of hormonal stimulation of ovulation. The control group included 14 patients without thrombophilia and hemostasis disorders, but also participating in the IVF program due to the presence of tubal-peritoneal and male infertility factors. The number of IVF cycles was no more than three. The study did not include patients with other infertility factors other than tubal-peritoneal and male factors, multiple pregnancies, aggravated somatic anamnesis. All pregnant women were comparable in terms of anamnesis, reproductive function and age.

The examination was performed at the time from the beginning of ovulation stimulation to delivery every 4 weeks.

In addition to general clinical studies, all patients underwent: ultrasound examination (ultrasound) with dopplerometry in the early stages of gestation (examination of blood flow in the uterine, spiral arteries, venous duct, the yolk duct, in the yolk sac, the index of the venous duct, blood flow in the interstitial space). Markers of antiphospholipid syndrome (AFS), antibodies to human chorionic gonadotropin (hCG), genetic forms of thrombophilia were studied: mutation of Leiden factor V, prothrombin gene, methylenetetrahydrofolate reductase and plasminogen activator gene, TORCH complex studies and prenatal screenings in the I and II trimesters of pregnancy, hemostasis system study: fibrinogen indicators were determined, activated partial thromboplastin time, activated recalcification time, prothrombin index, D-dimer, platelet aggregation activity.

Of the examined patients, 32 (60.2%) were pre-pregnant, 21 (39.8%) were repeat-pregnant, whose previous pregnancies were accompanied by complications such as the threat of termination, gestosis, fetoplacental insufficiency (FPI), complicated by fetal growth retardation syndrome (FGRS) (Fig. 1). Full-term delivery in 15 (71.4%) of patients out of 21 occurred through the natural birth

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canal, cesarean section after 36 weeks was performed only in 2 (28.6%) of 17 patients (both patients are in the comparison group) according to perinatal indications (FPI, FGRS).

We found that during three IVF cycles, pregnancy occurred in 41 out of 53 (76.9%) patients: in 18 (34.4%) patients with thrombophilia, in 18 (34.4%) - with hypercoagulation and in 16 (31.2%) - without hemostasis disorders. We found that in all women with thrombophilia and chronic DIC syndrome, the course of pregnancy in the first trimester was 100% complicated by the threat of termination. All patients complained of pulling pains in the lower abdomen, and bloody discharge from the genital tract was noted by 59.4%. At the same time, pregnancy in the first trimester (up to 12 weeks) in the first the group was interrupted by 15.6%, 10.9% in the second and 6.3% in the third groups. It should be noted that the percentage of non-developing pregnancies in the groups with thrombophilia and hypercoagulation was 70% and 68%, respectively. As pregnancy progressed, there was a significant highest percentage of the development of AF and gestosis in patients with thrombophilia and chronic DIC syndrome.

We found that in groups with thrombophilia and hypercoagulation, there is also an increase in platelet aggregation activity. In the control group, there were also changes in the hemostasiogram, but they were adaptive in nature and additional drug correction was not performed in pregnant women.

In case of pregnancy complications (gestosis, AFN, NWRP), all patients underwent comprehensive pathogenetic and symptomatic therapy based on modern principles of treatment of the identified pathology.

Results and Discussion

Given the low rates of pregnancy after the first IVF cycle, additional risk factors for non-pregnancy were identified, which included thrombophilia and hypercoagulation in the hemostasis system.

According to our data, a low percentage of pregnancy was detected in pregnant women with thrombophilia, they underwent anticoagulant therapy by subcutaneous administration of low molecular weight heparin (NMH). As a result

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of the treatment in the repeated IVF cycle, pregnancy rates increased from 6.7% to 30%. Pregnancy progressed under the control of a hemostasiogram in patients with thrombophilia. The study of the levels of soluble receptor of vascular endothelial growth factor 1 (sRVEGF 1) and placental growth factor (PlGF) showed a significant slow increase in blood plasma during the 1st and 2nd trimester of pregnancy in all groups.

However, the level of soluble vascular endothelial growth factor receptor 1 in the group with thrombophilia is 1.3 times higher than in pregnant women without hemostasis disorders, while the level of placental growth factor is 1.3 times lower than in patients with physiological pregnancy.

66.7% of patients with thrombophilia and retrochorial hematoma up to 20 mm had spontaneous miscarriage and 33.3% had an undeveloped pregnancy. In one pregnant woman with hypercoagulation on the background of retrochorial hematoma there was a spontaneous miscarriage. No reproductive losses were observed in retrochorial hematoma up to 10 mm in size. Since the most intense vascularization of the yolk sac was noted in the first trimester of pregnancy, when determining blood flow disorders in the mother-placenta-fetus system, we found that pregnant women with thrombophilia had blood flow disorders in the interstitial space towards an increase in vascular resistance (resistance index (IR) and pulse index (PI)) at the age of 8-12 weeks (YR=0,52 +/- 0,03 , PI=0,73 +/- 0,05) pregnancy in 58.3%, with hypercoagulation - in 33.3%, without violations of the hemostasis system - in 25%. Violations of blood flow in the yolk duct in the direction of increase (IR= 0,60 +/- 0,04 , PI= 1,20 +/- 0,06) in the same ratio. When determining the blood flow in the vessels of the yolk sac, arterial character was revealed in all examined pregnant women, which corresponds to the normative indicators.

The study of blood flow velocity curves in uterine arteries (UA) and spiral arteries (SpA) has established certain patterns of development of pregnancy complications in the 2nd and 3rd trimesters of pregnancy. The analysis carried out

The results of the Doppler study showed that with an increase in the values of vascular resistance indices in the SpA at the end of the first trimester (IR more

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than 0.42), it leads to the development of gestosis and AF. In almost 85% of the subjects in the first trimester in all groups (n= 16), in whom pregnancy was complicated by AF and gestosis, a violation of blood flow in the SpA was noted, and subsequently a one- and two-way increase in MA was established (systolic-diastolic ratio of MA more than 2.4).

We noted that in patients with thrombophilia and complicated course of the 1st trimester of pregnancy after IVF (threat of miscarriage, chorion detachment and retrochorial hematoma) in 30% of cases, the sVEGFR1 index was significantly lower than in patients with chronic DIC syndrome and without hemostasis disorders. In case of violation of uteroplacental blood flow towards increased vascular resistance, changes in the parameters of angiogenic growth factors in blood plasma, namely, an increase in the level of soluble vascular-endothelial receptor 1 and an increase in the level of placental growth factors

This led to the development of complications such as gestosis and PN in pregnant women with thrombophilia in 41.7% and 66.7%, in patients with chronic DIC syndrome in 40% and 46.7% and in women without hemostasis disorders in 25% and 33.3%, respectively.

Taking into account the peculiarities of the anamnesis, as well as the presence of complications during pregnancy, 37 (86%) of 43 patients were delivered by cesarean section. Indications for surgery were the presence of a scar on the uterus after cesarean section and the inability to rule out its failure in childbirth (2 patients in the group with hypercoagulation), severe gestosis the degree and lack of effect of the therapy, high myopia, narrowing of the pelvis and large fetal size, however, in most cases, long-term infertility and the age of primiparous women over 30 years served as an indication for cesarean section surgery. Premature birth occurred in 34.9% of patients: 20.9% in the main group, 9.3% in the comparison group and 4.7% in the control group; this complication was detected in women with severe gestosis and PI, premature outpouring of water. All operations proceeded without technical difficulties, blood loss during the operation averaged 576,89 +/- 53,3 Six pregnant women of the control group were delivered through the natural birth canal, taking into account the presence of a history of childbirth,

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the absence of a burdened somatic history and a normal pregnancy. All deliveries were uneventful, and blood loss during childbirth averaged 154,4 +/- 32,6 ml.
The early and late postpartum periods also proceeded without complications. The absence of hemorrhagic complications during delivery is more likely to be associated with timely correction of hemostatic disorders.
Thus, in women after ART, a comprehensive examination is necessary, starting from the first trimester of pregnancy, which, in addition to ultrasound, includes the determination of thrombophilic status and angiogenic growth factors.
A decrease in the level of PlGF indices, an increase in sVEGFR1 values, and a violation of uteroplacental blood flow during Dopplerometry in the first trimester of pregnancy makes it possible to identify risk factors for the development of the threat of termination of pregnancy, PI and gestosis. Timely diagnosis of hemostatic system disorders and determination of the level of angiogenic factors allows for preventive and pathogenetically justified, differentiated therapy, which will reduce the incidence of pregnancy complications after IVF.

References

1. Стрижаков А.Н. Потеря беременности / А.Н. Стрижаков, И.В. Игнатко. — М.: «Медицинское информационное агентство», 2007. — 224 с.
2. Тимохина Е.В. Синдром задержки роста плода: патогенез, прогнозирование, акушерская тактика: автореферат дис. ... доктора медицинских наук: 14.01.01 / Москва, 2012. - 48 с.
3. Kumazaki, K. Expression of vascular endothelial growth factor, placental growth factor, and their receptors Flt-1 and KDR in human placenta under pathologic conditions / K. Kumazaki [et al.] //Hum. Pathol. -2002. -Vol. 33; No11.-p. 1069-1077.
4. Bartha, J.L. Fluman chorionic gonadotropin and vascular endothelial growth factor in normal and complicated pregnancies [Text]/ J.L. Bartha [et al.] //Obstet. Gynecol. - 2003. - Vol.5. - p.995-999.
5. Espinoza, J. Unexplained fetal death: another anti-angiogenic state / J. Espinoza [et al.] // J. Matern. Fetal. Neonatal. Med. - 2007. - Vol. 20; No 7. - p. 495 - 507.

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ISSN (E): 3067-803X
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Website: usajournals.org

6. Wallner, W. Angiogenic growth factors in maternal and fetal serum in pregnancies complicated by intrauterine growth restriction / W. Wallner [et al.] //Clin. Sci. (Lond). -2007.- vol.112; No1.- p.51-57.
7. Фадеева Н.И. Кравцова Е.С.Лечение пациенток с угрозой прерывания беременности и профилактика первичной плацентарной недостаточности при частичной отслойке хориона в эмбриональной стадии развития плодного яйца // Российский вестник акушера-гинеколога http://www.mediasphera.ru/journals/akuvest/detail/83/765/
8. Кирющенков П.А., Белоусов Д.М., Александрина О.С. Патогенетическое обоснование тактики ведения отслойки хориона и плаценты на ранних сроках беременности // Гинекология. – 2010. – Т. 12, № 1. – С. 36–39.
9. Милованов, А.П. Патология системы мать-плацента-плод: Руководство для врачей / А.П. Милованов. -М.: Медицина, 1999.- С. 293, 366.
10. Zygmynt, M. Angiogenesis and vasculogenesis in pregnancy / M. Zygmynt [et al.]//Obstst.Gynecol.-2003.-Vol. 110.-No3.-P.10-18.
11. Пономарева, А.Ю. Роль ангиогенных факторов роста, эндотелина-1 и нейрокинина Б в генезе гестоза : дис. ...канд. мед. наук: 14.00.01/ ФГУ Ростовский НИИ акушерства и педиатрии; Пономарева Алла Юрьевна; науч. рук. В.И. Орлов. - Ростов - на - Дону, 2006.-159С. - Библиогр.: С. 135-159.
12. Макацария А.Д., Бицадзе В.О. Тромбофилии и противотромботическая терапии в акушерской практике. М.: Триада-Х, 2003. - 904 с .
13. Макацария А.Д., Бицадзе В.О., Акиньшина С.В. Тромбозы и тромбоэмболии в акушерско-гинекологической клинике. Молекулярно-генетические механизмы и стратегия профилактики тромбоэмболических осложнений: Рук. для врачей. Москва, МИА, 2007г.
14. Khamashta, M A, Ruiz-Irastorza, G Systematic lupus erythematosus and antiphospholipid syndrome during pregnancy // Zeitschrift für Rheumatologie 05/2006
15. Martinelli I. Prothrombin A19911G polymorphism and the risk of venous thromboembolism / Martinelli I., Battaglioli T., Tosetto A., Legnani C., Sottile1., Ghiotto R., Mannucci P.M. // J. Thromb. Haemost.- 2006.- 4(12).-2582-2586.

Modern American Journal of Medical and Health Sciences
ISSN (E): 3067-803X
Volume 01, Issue 09, December, 2025
Website: usajournals.org

16. Кузнецова, В.С. Особенности адаптации в раннем неонатальном периоде новорожденных детей, рожденных у женщин с бесплодием в анамнезе после циклов экстракорпорального оплодотворения / В.С. Кузнецова, И.И. Логвинова, И.Н. Коротких // Журнал практической и теоретической медицины. – 2004. – Т. 2, № 1. – С. 59-62.
17. Богачева, Н. А., & Пицхелаури, Е. Г. (2014). Роль ангиогенных факторов и показателей системы гемостаза в прогнозировании осложнений беременности после ВРТ. Международный научно-исследовательский журнал, (8-3 (27)), 6.