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EVALUATION OF BIOCHEMICAL AND ULTRASOUND MARKERS FOR PREDICTING THE DEVELOPMENT OF PREECLAMPSIA

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✓ ***Resume***

Preeclampsia (PE) occupies one of the most important places among the problems of scientific and practical obstetrics, the frequency of which, according to WHO data, can reach up to 28% among pregnant women, thereby representing the main part of hypertensive conditions during pregnancy. Moreover, severe PE occurs in 1.3 - 6.7% of pregnant women. Preeclampsia is diagnosed after the 20th week of pregnancy. Complications that can be fatal include premature placental abruption, disseminated intravascular coagulation (DIC), cerebral hemorrhage, liver failure, and acute renal failure. This review focuses on biochemical and ultrasound markers of high risk of preeclampsia. Of particular interest is the balance of proangiogenic (PIGF) and antiangiogenic (sFlt) growth factors at different stages of pregnancy; correct interpretation of the sFlt/PIGF ratio and correlation with anamnesis data already allows expanding the criteria for the prevention of preeclampsia and opens up prospects for optimizing obstetric tactics in the third trimester of pregnancy.

Key words: preeclampsia, early diagnosis of preeclampsia, biochemical markers of preeclampsia, ultrasound markers of preeclampsia, sFlt-1/PlGF, placental growth factor (PIGF), pulsatility index of the uterine arteries

ОЦЕНКА БИОХИМИЧЕСКИХ И УЛЬТРАЗВУКОВЫХ МАРКЕРОВ ПРЕДИКЦИИ РАЗВИТИЯ ПРЕЭКЛАМСИИ

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✓ ***Резюме***

Преэклампсия (ПЭ) занимает среди проблем научного и практического акушерства одно из важнейших мест, частота которой, согласно данным ВОЗ, может достигать до 28% среди беременных, тем самым представляя собой основную часть гипертензивных состояний во время беременности. Более того ПЭ тяжелой формы встречается у 1,3 - 6,7% беременных женщин. Преэклампсию выявляют после 20 недели беременности. Осложнения, которые могут привести к летальному исходу, запускают преждевременную отслойку плаценты, диссеминированное внутрисосудистое свертывание (ДВС) крови, кровоизлияние в мозг, печеночную недостаточность и острую почечную недостаточность. Данный обзор посвящен биохимическим и ультразвуковым маркерам высокого риска развития преэклампсии. Особый интерес представляет баланс проангиогенных (PIGF) и антиангиогенных (sFlt) факторов роста на разных сроках беременности; правильное толкование соотношения sFlt/PIGF и соотношение с данными анамнеза уже позволяют расширять критерии профилактики преэклампсии и открывают перспективы оптимизации акушерской тактики в III триместре беременности.

Ключевые слова: преэклампсия, ранняя диагностика преэклампсии, биохимические маркеры преэклампсии, ультразвуковые маркеры преэклампсии, sFlt-1/PlGF, плацентарный фактор роста (PIGF), пульсационный индекс маточных артерий

PREEKLAMSIYA RIVOJINI BASHORAT QILISH UCHUN BIOKIMYOVIY VA ULTRATOVUSHLI MARKERLARNI BAHOLASH

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✓ ***Rezyume***

Preeklampsiya (PE) ilmiy va amaliy akusherlik muammolari orasida eng muhim o'rinlardan birini egallaydi, JSST ma'lumotlariga ko'ra, homilador ayollarda tez-tezligi 28% gacha yetishi mumkin va shu bilan homiladorlik davridagi gipertenziv holatlarning asosiy qismini tashkil qiladi. homiladorlik. Bundan tashqari, og'ir PE homilador ayollarning 1,3-6,7 foizida uchraydi. Preeklampsi homiladorlikning 20-haftasidan keyin aniqlanadi. O'limga olib kelishi mumkin bo'lgan asoratlarga platsentaning erta ajralishi, tarqalgan intravaskulyar koagulyatsiya (DIC), miya qon ketishi, jigar etishmovchiligi va o'tkir buyrak etishmovchiligi kiradi. Ushbu sharh preeklampsi xavfi yuqori bo'lgan biokimyoviy va ultratovush belgilariga qaratilgan. Homiladorlikning turli bosqichlarida proangiogen (PIGF) va antiangiogen (sFlt) o'sish omillarining muvozanati alohida qiziqish uyg'otadi; sFlt / PIGF nisbati va anamnez ma'lumotlari bilan korrelyatsiyani to'g'ri talqin qilish allaqachon preeklampsiyaning oldini olish mezonlarini kengaytirishga imkon beradi va homiladorlikning uchinchi trimestrida akusherlik taktikasini optimallashtirish istiqbollarini ochadi.

Kalit so'zlar: preeklampsi, preeklampsiyaning erta tashxisi, preeklampsiyaning biokimyoviy belgilari, preeklampsiyaning ultratovush belgilari, sFlt-1/PlGF, platsenta o'sish omili (PIGF), bachadon arteriyalarining pulsatsiyalanish indeksi

Relevance

Preeclampsia (PE) is understood as a complication of pregnancy, which is determined by a discrepancy in the ability of the maternal body's adaptive systems to meet the needs of the developing fetus. In this case, there is a syndrome of multiple organ failure that develops during pregnancy, which disappears after childbirth. This pathological condition develops after the 20th week of pregnancy and is manifested by the appearance of arterial hypertension ≥ 140/90 mmHg. Art. in combination with proteinuria

(≥ 0.3 g/day), in addition to the specified multisystem failure. To date, no single definite theory of the etiology and pathogenesis of preeclampsia has been identified, which may be the result of the presence of various trigger mechanisms. Experts studying PE believe that based on clinical parameters, hemodynamic changes, biochemical and ultrasound predictors, the risk of developing preeclampsia in the first trimester of pregnancy can be predicted.

The purpose of our study was to study biochemical and ultrasound markers for predicting the development of preeclampsia.

Materials and methods

The study was conducted on the basis of the Republican Specialized Scientific and Practical Medical Center of Obstetrics and Gynecology, 55 women, aged 24±1.2 years, who applied to the center's clinic with a gestational age of 10.5±1.7 weeks, were examined. All patients underwent an ultrasound examination to determine the pulsatility index of the uterine arteries and analyzes of PlGF - placental growth factor , sFlt-1 - soluble fms-like tyrosine kinase-1 , and calculation of the sFlt-1/PlGF ratio

Result and discussions

The concentration of PlGF and sFlt-1 in the blood serum of pregnant women was determined using electrochemiluminescent diagnostic test systems Elecsys PlGF and Elecsys sFlt-1 from the Hoffmann La Roche concern (Switzerland) on a Cobas e411 automatic analyzer from the same company. The following were examined:

• in the first trimester – 18 patients with a physiological pregnancy period of 11–13 weeks, who, according to ultrasound data, had a normally developing fetus and a low risk of fetal pathology according to the results of prenatal diagnosis;

• in the second trimester – 12 patients with a physiological pregnancy period of 16–20 weeks, without pathologies of fetal development;

• in the third trimester of pregnancy – 25 patients with a physiological pregnancy period of 30–39 weeks, without pathology of fetal development.

Blood was obtained from the antecubital vein. The blood pressure level in all patients during pregnancy did not exceed the normative range, and protein in the urine was not recorded.

In the first trimester of pregnancy, the concentration of PlGF is significantly lower than that in the second trimester of pregnancy, and the concentrations of sFlt-1 do not differ significantly. The sFlt-1/PlGF ratio in the first trimester was 39.3±4.2. The concentrations of PlGF and sFlt-1 at 16 weeks did not differ significantly from the corresponding indicators at 17 and 18 weeks of pregnancy. At 19 weeks, the concentration of PlFG significantly increased, and at 20 weeks it significantly exceeded that at 19 weeks. The ratio of the concentrations of PlGF and sFlt-1 changed accordingly. At 16–18 weeks of pregnancy, the sFlt-1/PlGF ratio averaged 13.1±2.6, while at 19–20 weeks it was 6.9±2.1. It should be especially noted that in the first trimester of pregnancy (11–13 weeks) the average value of this indicator was 39.3±4.2. During the third trimester of pregnancy, the following features of the dynamics of PlGF and sFlt-1 concentrations were noted. At 30–32 weeks, the concentration of PlGF was more than 2 times higher than that at 20 weeks of pregnancy, and the concentrations of sFlt-1 at these stages of pregnancy did not differ significantly. Accordingly, the sFlt-1/PlGF ratio at 30–32 weeks was minimal and averaged 1.7±0.8. According to the literature, similar results were obtained by a group of researchers from the Department of Obstetrics and Hospital at the University of Leipzig, Germany [12]. At 33–36 weeks of pregnancy, the concentration of PlGF was 3 times lower than that at 30–32 weeks, and the concentration of sFlt-1 increased 2 times. The ratio of these indicators was 10±2.5. At 37–40 weeks of pregnancy, a further decrease in the concentration of PlGF and an increase in the concentration of sFlt-1. Their ratio was 17.6±2.4. These results are also consistent with published data [12, 13]. Thus, as a result of the work carried out, data were obtained on the content of PlGF, sFlt-1 and the values of their ratio in pregnancy periods from 11 to 13 weeks, from 16 to 20 weeks and from 30 to 40 weeks.

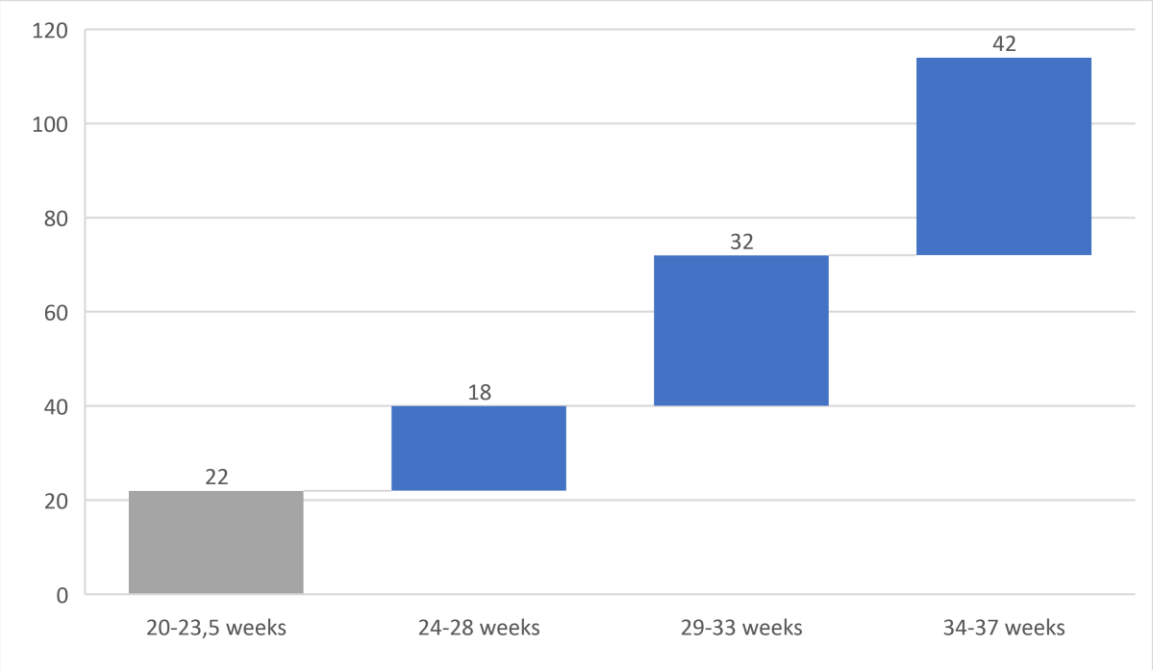

Fig. 2 The ratio of the content of soluble fms -like thyroxinase-1 and placental growth factor (sFlt -1/PlGF) depending on the duration of pregnancy

In the study group of patients who subsequently developed preeclampsia, a decrease in PlGF concentration was noted already at 11–16 weeks of gestation. The borderline level of PlGF, which is the

border between a normal pregnancy and preeclampsia, at 12–13 weeks of pregnancy is 42.7 ± 23.2 pg/ml (without signs of preeclampsia - 80.6 ± 35.2 pg/ml). Thus, a prognostic marker of preeclampsia is the level of PlGF in the blood serum of 50–100 pg /ml, which serves as an early valuable marker in the diagnosis of this disease and shows initial signs of disturbances in the fetoplacental complex, occurring long before clinical placental insufficiency. The study found an association between elevated sFlt - 1 levels and preeclampsia. Already 5–6 weeks before the onset of PE, sFlt - 1 levels increase and remain elevated compared to normal physiological pregnancy. Determining the content of PlGF and sFlt - 1 in the maternal bloodstream allows us to predict the development of preeclampsia, since these indicators reflect the imbalance between proangiogenic and antiangiogenic factors. A significant decrease in PlGF and an increase in the concentration of sFlt - 1 was found in pregnant women with PE compared to healthy pregnant women. Confirmation of PE is the limiting values of the ratio sFlt- 1/PlGF > 85 (gestational age from 20 + 0 to 35 + + 6 weeks) and sFlt -1/PlGF > 110 (34 + 0 weeks before birth). An increased sFlt - 1/PlGF ratio reflects the pathology of ineffective placentation, placental ischemia and is considered a promising biomarker for predicting and diagnosing the disease.

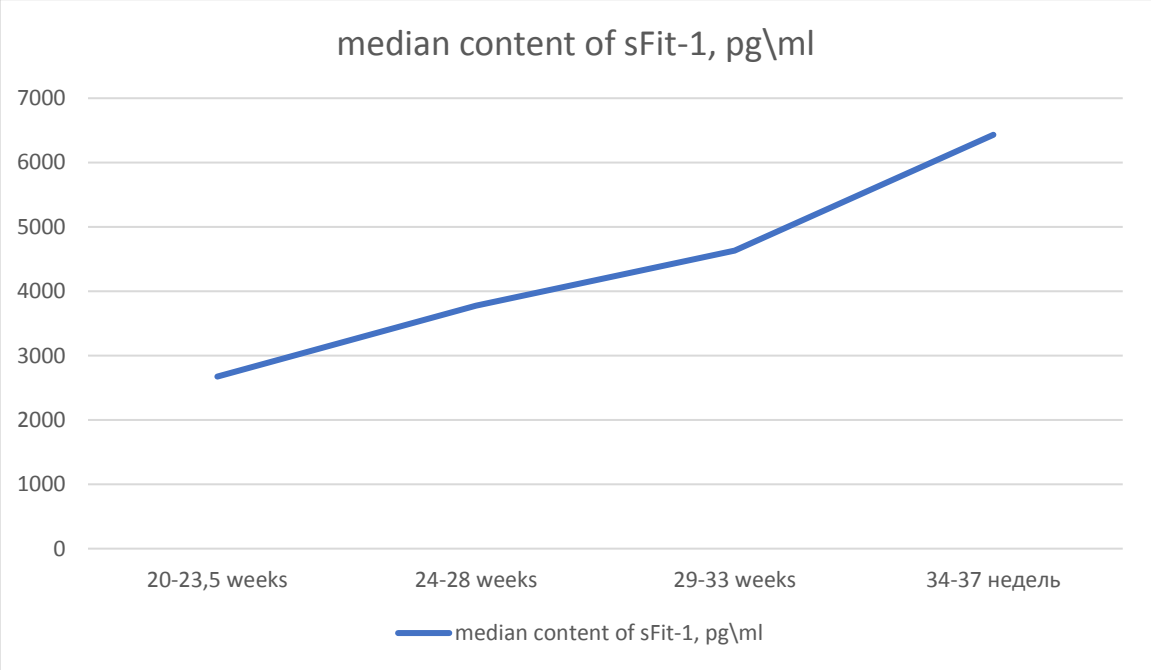

Fig. 1 Median content of soluble fms -like thyroxinase depending on the stage of pregnancy

The pregnancy periods chosen for the study are due to the fact that it is at this time that planned prenatal diagnostics are carried out, in the first and second trimesters, as well as dynamic monitoring of the condition of the fetus in the third trimester of pregnancy. It seems that assessing the risk of developing preeclampsia during these stages of pregnancy can help reduce the incidence of complications and perinatal losses, since taking appropriate measures in a number of cases makes it possible to timely correct the developing pathological condition and resolve the issue of timing of delivery.

Conclusions

The concentrations of sFlt-1 and PlGF, as well as their ratio, are highly informative indicators of preeclampsia. The determination of the concentration of these markers and the calculation of their ratio must be carried out in the first and second trimesters of pregnancy as part of a screening program for diagnosing intrauterine fetal pathology. This will allow us to resolve the issue of the advisability of maintaining this pregnancy and tactics for preventing the development of preeclampsia. Determination of markers of preeclampsia in the third trimester of pregnancy can serve as the basis for the final diagnosis and decision on the timing of delivery in order to preserve the life of the woman and the fetus. Assessing the threat of developing PE in the early stages will contribute to the development of an adequate treatment algorithm to eliminate the risk of death for both the mother and and for the fetus.

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