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INDICATORS OF ANGIOGENESIS IN PREGNANT WOMEN WITH ARTERIAL HYPERTENSION

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Summary. The role of the factors of angiogenesis and hormones of pregnancy in pregnant women with hypertension has been studied inadequately and their interaction in such patients is not fully elucidated at present time. **Aim.** To detect peculiarities of angiogenesis factors and placental hormones in pregnant women with arterial hypertension I and II grades in comparison with results of healthy pregnant women. **Materials and methods.** Conducting a prospective study of 88 pregnant women, which included: analysis of clinical and anamnestic characteristics and study of the peculiarities of pregnancy in women with chronic hypertension in the first trimester of pregnancy (11-12 weeks). The open prospective controlled study involved 61 pregnant women with chronic arterial hypertension (CAH) 1-2 degree, who were included in the first - the main group. The second control group included 27 healthy pregnant women with physiological pregnancies. Among the angiogenesis indices, the placental growth factor (PlGF), as a pro-angiogenic factor and placental soluble fms-like tyrosine kinase (sFlt-1) was determined as an anti-angiogenic factor, sFlt-1/PlGF ratio was also estimated. Statistical analysis was done by using «STATISTICA® for Windows 6.0» (Stat Soft Inc., № AXXR712D833214FAN5). **Results.** In the first trimester of pregnancy (11-12 weeks of gestation) in women with CAH is determined by a shift in the balance between pro- and antiangiogenic factors, manifested by statistically significant ($p < 0.05$) increase in sFlt-1 levels (1700, 9 pg / ml) and a decrease in PlGF levels in 3.7 times (9.1 pg / ml) and, accordingly, an increase in the levels of the coefficient K in 5.3 times (sFlt-1 / PlGF) (184.5). The mean values of estradiol,

*progesterone and chorionic gonadotropin levels in pregnant women with CAH did not differ statistically significantly from those of the control group ($p>0.05$). These changes indicate the presence of angiogenesis disorders in pregnant women with chronic hypertension, starting from the first trimester of gestation. **Conclusions.** Pregnant women with CAH in 1 trimester have disturbances in balance between pro-angiogenic and anti-angiogenic factors with prevalence of sFlt-1 and reducing of PlGF in serum plasma. Due to such disbalance in pregnant women with CAH of 1 and 2 grade changed cooperation between angiogenesis factors and hormones from direct to inverse. It may lead to development of placental insufficiency in future. That's why treatment/prophylaxis of it should be administered to pregnant women with CAH in 1 trimester.*

Keywords: factors of angiogenesis, pregnancy, arterial hypertension.

Arterial hypertension (AH) occupies a leading position among these cardiovascular diseases. AH promotes the development of long-term vascular and metabolic disorders [1]. There is a decrease in placental blood flow in pregnant women with AH due to changes in the functioning of the cardiovascular system. Disturbances of the normal relationship between vasodilators and vasoconstrictors in pregnant women with AH are accompanied by dysregulation of vascular tone and leads to placental insufficiency [2]. The activity of placental angiogenesis is controlled by a spectrum of growth factors with pro-angiogenic and anti-angiogenic properties [3, 4, 5, 6]. The placental growth factor (PlGF) in the first trimester of pregnancy stimulates the synthesis of trophoblastic DNA, increases the number of trophoblast cells and improves the conditions for its infestation [7, 8, 9, 10]. Anti-angiogenic factors include placental soluble fms-like tyrosine kinase (sFlt-1) [11]. It counteracts the action of PlGF on specific receptors [12]. The imbalance between pro- and anti-angiogenic factors contributes to placental insufficiency [4, 6, 12]. The role of the factors of angiogenesis of pregnancy in pregnant women with hypertension has been studied inadequately and their interaction in such patients is not fully elucidated at present time.

Aim: to detect peculiarities of angiogenesis factors in pregnant women with arterial hypertension.

Materials and methods. Conducting a prospective study of 88 pregnant women, which included: analysis of clinical and anamnestic characteristics and study of the peculiarities of pregnancy in women with chronic hypertension in the first trimester of pregnancy (11-12 weeks). In the dynamics of pregnancy, all patients were examined by a physician. According to the indications of pregnant women, consultations of specialists of other specialties were carried out and additional instrumental research methods were performed.

The open prospective controlled study involved 61 pregnant women with CAH 1-2 degrees, who were included in the first – the main group (mean age was 27.7 ± 1.7 years). The second control group included 27 healthy pregnant women with physiological pregnancies (mean age – 27.9 ± 1.4). Anamnesis, general clinical examination, measured of blood pressure, standard obstetric and gynecological examination according to clinical protocols were done in all cases. The evaluation of the outcome of the accouchement was performed on the assessment of the fetal condition on the Apgar scale, weight of the fetus. AH was diagnosed according to the existing clinical protocols.

Among the markers of angiogenesis in blood serum, the following were determined: the placental growth factor (PGF), as a pro-angiogenic factor and

placental soluble fms-like tyrosine kinase (sFlt-1) was determined as an anti-angiogenic factor, sFlt-1/PGF ratio was also estimated. Research of hormones and factors of angiogenesis was performed on the basis of the Educational Medical Laboratory Center of the Zaporizhzhya State Medical University. For this purpose, the full-wave enzyme-linked enzyme analyzer Sirio-S (Seac, Italy) was used. Statistical analysis was done by using «STATISTICA® for Windows 13.0».

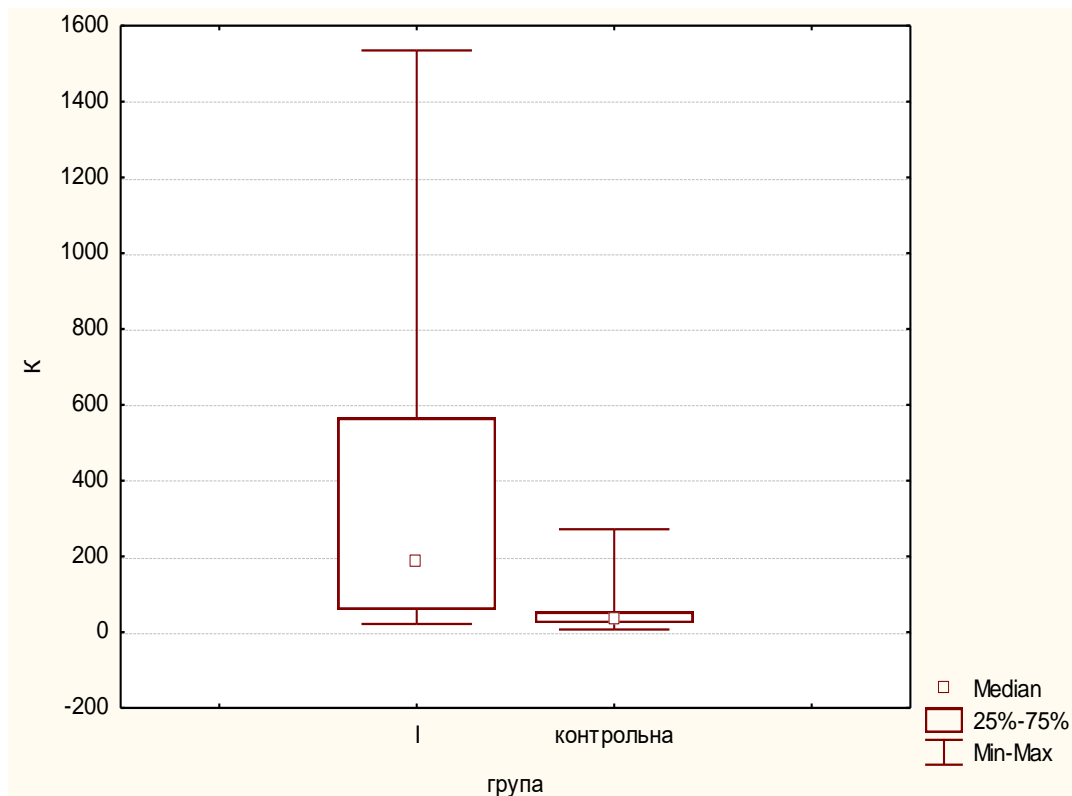
Results. We could say that assessing the average levels of angiogenic factors, found a statistically significant difference between the groups, $p > 0,05$. (tab. 1).

Table 1

Levels of angiogenesis in groups of pregnant women

| Indexes | I group, n=61 Me (Q ₂₅ ;Q ₇₅) | control group, n=27 Me (Q ₂₅ ;Q ₇₅) | P |
|---------------|---|---|--------|
| PIGF, pg/ml | 9,1 (3,8;19,2) | 33,6 (26,8;45,6) | <0,001 |
| sFlt-1, pg/ml | 1700,9 (1315,6;2005,6) | 1419,7 (1060,3;1673,5) | <0,05 |
| K | 184,5 (59,5;565,3) | 34,7 (24,1;53,7) | <0,001 |

It was found that the level of PIGF was significantly reduced in persons of group I 3.7 times: 9.1 (3.8; 19.2) pg / ml against 33.6 (26.8; 45.6) pg / ml in women of the II group, $p < 0,001$. The rate of sFlt-1, in contrast, was higher in pregnant women with CAH: 1700.9 (1315.6; 2005.6) pg / ml against 1419.7 (1060.3; 1673.5) pg / ml, $p < 0,05$. Given the changes in the markers of angiogenesis, it was decided to calculate the ratio of these factors (soluble fms-like tyrosine kinase to placental growth factor) to each other. The ratio of sFlt-1 to PIGF was denoted by the coefficient K. Accordingly, K was significantly increased in persons of group I in 5.3 times: 184.5 (59.5; 565.3) units against 34.7 (24.1; 53.7) units, $p < 0,001$. (pic. 1)



Picture 1. Levels of angiogenesis (coefficient K) in groups of pregnant women

Conclusions. Thus, it was found that in the first trimester of pregnancy (11-12 weeks of gestation) in women with CAH is determined by a shift in the balance between pro- and antiangiogenic factors, manifested by statistically significant ($p < 0.05$) increase in sFlt-1 levels (1700, 9 pg / ml) and a decrease in PlGF levels in 3.7 times (9.1 pg / ml) and, accordingly, an increase in the levels of the coefficient K in 5.3 times (sFlt-1 / PlGF) (184.5).

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