

Conflict of interest: None declared. Received: 15.10.2013. Revised: 15.11.2013. Accepted: 20.12.2013.

The role of endothelial dysfunction for pregnancy complications occurrence with asiderotic anemia in pregnant women

Ancheva I.A.

Odessa National Medical University

Iron-deficiency anemia (IDA) is one of the key problems of obstetrics due to the wide spread occurrence and high frequency of obstetrical and perinatal complications development [1]. According to WHO the IDA frequency in pregnant women is up to 80%. Anemia causes a derangement of the basic erythrocytes' function – oxygen transportation, which is the reason for hemic and secondary tissular hypoxia development, which injures endothelium and leads to its dysfunction [1, 2]. Endothelial dysfunction is a pathologic state of the endothelium, based on the endothelial factors production disorder, due to which there is unable to make hemorheological and immunoinert blood balance, which causes complex dysfunction in the “mother-placenta-fetus” system during the pregnancy. The dysfunction of the endothelium causes disorder in microcirculation in the placenta and hampers the normal pregnancy [3].

During a physiological pregnancy the stimulation and activation of fetoplacental complex is observed which leads to almost twice coagulating potential increasing. On the background of fibrinolytic and antycoagulating activity decreasing the content of all factors of turning increases. Beginning from the third trimester of the pregnancy the increasing of production by endothelium and secretion of Willebrand's factor, thromboxane, endothelin-1, thrombomodulin and fibronectin is registered, so certain phenomena which are inherited to endothelial dysfunction syndrome appear even during physiological course of pregnancy[3, 4] .

However, till recent time the investigation of endothelial dysfunction's influence upon the pregnancy with combination of IDA and placental dysfunction was not paid much attention. But endothelial dysfunction is a universal defect of the wall of a vessel. It has been proved that endothelium of the bloodstream carrying out local mediators' synthesis takes part in a vascular tone regulation, secures hemostasis, immune response, blood cells migration into the vessel wall, synthesis of inflammation factors and their inhibitors, carries out barrier functions. An imbalance between mediators which normally provide an optimal course of endothelium depending processes is the main link of pathogenesis of many pregnancy complications[5].

The aim of the investigation was the estimation of endothelium state in pregnant women who suffer with asiderotic anemia.

The material and the methods of the investigation.

The investigation is held on the base of the city maternity hospital #2 during the 2013 year. There were investigated 20 pregnant women with manifestations of anemia and placental dysfunction in the 28-36 weeks' term of the pregnancy according to the order of Ministry of Health of Ukraine №782 from 2005.12.29 «About the affirmation of clinical protocols of obstetrical and gynecological help» [6]. For the control there were investigated 20 pregnant women with the physiological course of pregnancy. The age range of the pregnant women was from 20 to 35 years old (in average $27,4 \pm 1,8$ years), most of them (75.0%) were in a registered marriage, 65,0% had completed higher education.

Also the endothelial function was estimated with duplex scanning the brachial artery with a linear measuring devise with high resolution using tests with reactive hyperemia and nitroglycerin.

There was used echolocation with high resolution and Dopler echocardiography of the brachial artery which was done by Celermajer D.S. et al. (1992) method before and after the temporary occlusion the artery with the tonometer's cuff [7]. The brachial artery was located in a longitudinal section 2-10 cm upper of the bend of elbow. The diameter of the brachial artery was measured at a fixed distance between the middle and the adventitious layers of the artery. The investigation was done three times. Simultaneously a monitoring of the speed indices of the blood flow was held. Then a pneumatic cuff was put on the shoulder upper the measuring zone and was pumped to 50 mm of the mercury column upper of the systolic pressure of the pregnant woman. The duration of the phase of occlusion was 4 minutes. The dynamic estimation of the a. brachialis diameter and quantitative parameters of the blood flow were done at the 30th, 90th second and at the на 3rd, 5th and 7th minute after decompression. There were defined a. Brachialis diameter, peak systolic speed, and maximal usual diastolic speed before and after the test. Endothelium dependant vasodilatation was calculated as a ratio of the diameter of the artery with reactive hyperemia to the diameter of the artery in a calm state and was expressed in per cents. The speed indices changes were also calculated in per cents.

The ultrasound doplerometric investigation was done in the medical center "Opticor" (Odessa).

The statistic processing of the received data was done with a package of programs Statistica 10.0 (StatSoft Inc., USA) [8].

The results of private investigations.

During estimating individual data of reproductive anamnesis of the investigated women the following was determined. 60% of investigated women were first time pregnant, 20% women had had spontaneous abortions, 15% - artificial ones. One woman had had an extrauterine pregnancy. In some cases the pregnancy in patients was on the background of various gynecological diseases, such as epithelium of the neck of uterus dysplasia (15%), inflammatory diseases of pelvis minor organs (10%). One woman had a cicatrix on the uterus.

During analysis of the concomitant pathology there was determined that 4 women (20,0%) had a vira hepatitis A in the anamnesis, 10% – hepatitis B. One woman (5,0%) was overweight, 3 women (15,0%) had a chronic pyelonephritis, 2 women (10,0%) had a urolithiasis, there was a chronic bronchitis in some cases, a chronic gastritis, varicose diseases, hemorrhoid, high level myopia. The most of the pregnant women with IDA and placenta deficiency had high titer of causative aents of chronic infections including CMV (35,0%), HSV (45,0%), clamidiosis (15,0%), toxoplasmosis (40,0%).

During estimating the serum iron content in pregnant women there was determined that this datum in average was $11,3 \pm 0,5$ $\mu\text{mole/l}$. Correspondingly, the transferrin level in the serum of the pregnant women with signs of anemia was $4,4 \pm 0,4$ g/l, and ferritin – $15,8 \pm 1,4$ mcg/l, which confirms the diagnosis of **диагноз** iron deficiency anemia (IDA).

Average magnitude of the blood pressure in the investigated pregnant women corresponded to the physiological norm, which is $104,8 \pm 2,7$ mm mercury column (systolic BP) and $64,5 \pm 2,5$ mm mercury column (diastolic BP), there was no significant asymmetry in the right and the left hand in the investigated women during measuring in the office, however in the right hand average magnitude of the blood pressure were 3-5 mm mercury column higher than in the left one. This phenomenon can be explained by anatomic peculiarities of brachiocephalic vessels of a man.

The same is about the dopplerographic ultrasound investigation indices (the chart 1).

The chart 1

The indices of ultrasound Doppler investigation of the regional blood flow in pregnant women with IDA and placental deficiency

The indices	The right hand		The left hand	
	Before the testing	After the testing	Before the testing	After the testing
The peak line velocity, ml/s	110,0 \pm 5,0	110,6 \pm 5,0	104,3 \pm 5,5	102,6 \pm 3,2
Average maximal	36,4 \pm 4,0	40,2 \pm 3,8	34,5 \pm 4,1	36,6 \pm 3,5

ЛШК				
IR, од.	0,82±0,03	0,80±0,03	0,81±0,03	0,83±0,03
PI, од.	3,54±0,67	2,64±0,37	3,50±0,82	2,68±0,33
The brachial artery diameter, the systole, mm	3,36±0,09	3,55±0,10	3,22±0,06	3,59±0,08*
The brachial artery diameter, diastole, mm	3,16±0,08	3,35±0,10	3,06±0,06	3,42±0,07*

The note: * - the difference with outlet state is statistically significant

As it is seen from the given data the basic differences ($p < 0,05$) were observed at the level of changing the brachial artery into the systole and into the diastole. Such asymmetry can be explained by the fact that the most amount of the pregnant women who took part in the investigation (85%) had signs of endothelial dysfunction, due to which the change of the brachial artery diameter was not more than 10%. While there were no cases of endothelial dysfunction detection among the pregnant women of the control group ($\chi^2=26,2$ $p < 0,05$), thus with the presence of the physiological pregnancy in normally functioning endothelium the balance between constrictor and dilatation mechanisms.

The estimation of the functional state of the endothelium with the help of the flow depending vasodilatation is an adequate non invasive method of estimation the nature of endothelial function in pregnant women and can be used as an early test for adequate correction of malfunctions of the mechanisms of vessel tonus regulation to support the proper homeostasis and for the prophylactics of the pregnancy and delivery complications and of the fetus and a newborn pathologies.

It is necessary to point out that yet at the implantation and trophoblast invasion processes stage certain regularities of endothelial-hemostasiologic interaction are formed. Their malfunctions with systemic and local hypoxia caused by IDA causes the placental dysfunction. Signs of endothelial dysfunction in the most of the pregnant women with the placental dysfunction can be an evidence of the fact that a malfunction of the trophoblast invasion processes doesn't cause a physiological reconstruction of the spiral arteries, thus they remain sensitive to pathological changes of the hemodynamics of the mother's organism during all the pregnancy term.

In general, the used method of estimation of the functional state of the endothelium with flow depending vasodilatation in pregnant women is found to be rather informative one. In our opinion it can be used as an early test for adequate correction of malfunctions of the mechanisms of vessel tonus regulation to support the proper homeostasis and for the prophylactics of the pregnancy and delivery complications and of the fetus and a newborn pathologies.

The conclusion:

1. With IDA and placental dysfunction combination 85% of pregnant women have signs of endothelial dysfunction in the form of asymmetrical reaction of endothelium for reactive hyperemia after mechanical influence upon the vessel wall and increasing of the brachial artery diameter more than 10%.
2. The estimation of the functional style of the endothelium with flow depending vasodilatation is an adequate non invasive method of estimation of the endothelial function nature in pregnant women.

Література:

1. Iron status and its determinants in a nationally representative sample of pregnant women. / Vandevijvere S, Amsalkhir S, Van Oyen H [et al.] // J Acad Nutr Diet. - 2013 – Vol. 113(5) – P. 659-666.
2. Iron Deficiency & Overload. NY, Humana, 2009 – 884 p.
3. Климов В.А. Эндотелий при физиологической беременности. / В.А. Климов // Акушерство и гинекология. – 2006 - №5 – С. 11—14.

4. Петрищев Н.Н. Физиология и патофизиология эндотелия. / Петрищев Н.Н., Власов Т.Д. / в сб.: Дисфункция эндотелия. Причины, механизмы, фармакологическая коррекция. (под ред. Н.Н. Петрищева) СПб., 2003 – С. 4-38
5. Климов В.А. Эндотелий фетоплацентарного комплекса при физиологическом и патологическом течении беременности / В.А. Климов // Акушерство и гинекология. - 2008. - №2. - С. 7-10.
6. Наказ МОЗ України №782 від 2005.12.29 «Про затвердження клінічних протоколів з акушерської та гінекологічної допомоги» Електронний ресурс. Режим доступу: http://www.moz.gov.ua/ua/portal/dn_20051229_782.html
7. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. / Celermajer DS, Sorensen KE, Gooch VM [et al.] // Lancet. 1992 Nov 7;340(8828):1111-5
8. Боровиков В.П. STATISTICA: Искусство анализа данных на компьютере. / В.П. Боровиков СПб.: Питер, 2003, 700 с.

Summary

The role of endothelial dysfunction for pregnancy complications occurrence with asiderotic anemia in pregnant women.

Ancheva I.A.

Odessa National Medical University, Odessa

The aim of the study was to assess the endothelium in pregnant women suffering from iron deficiency anemia . It is shown that the combination of IDA and placental dysfunction is associated with the signs of endothelial dysfunction in the form of asymmetric response of endothelium to reactive hyperemia after mechanical stress on the vascular wall and increase the diameter of the brachial artery by more than 10 % in 85 % of pregnant women. The data suggest that the assessment of the functional state of the endothelium via flow-dependent vasodilation is adequate non-invasive method of assessing the nature of endothelial function in pregnant women.

Keywords: iron deficiency anemia , placental dysfunction, endothelium , pregnancy diagnosis.