

Changes in Placental NO Levels During Physiological Pregnancy and Pregnancy Complicated with Eclampsia

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ABSTRACT

There are lots of evidences suggesting that various complications of preeclampsia, including vascular reactivity changes, vasospasm and multiorganic pathologies, occur due to the development of pathological changes in maternal vascular endothelium. There has been suggested that nitric oxide deficiency plays significant role in the development of structural and functional changes of vascular endothelium in maternal organism. Proceeding from aforesaid, our research aimed to study changes in placental NO levels during physiological pregnancy and pregnancy complicated with preeclampsia. As it proceeds from the analysis of literary data and the results obtained in our study, lowered free NO levels in placental tissue, detected by us during preeclampsia, may be due to eNOS gene mutation as well as to decreased expression of this enzyme and inhibition of iNOS synthesis. At the same time, significant elevation of nitrosylated hemoglobin (HbNO) levels in placenta during preeclampsia indicates the development of tissue hypoxia. Enhanced generation of HbNO complexes results in restriction of NO physiological function, placental dysfunction and aggravation of fetoplacental circulation deficiency.

KEYWORDS: *placenta, oxidative stress, nitric oxide, preeclampsia*

So far the etiology and pathogenesis of one of the frequent and dangerous complication of pregnancy, preeclampsia has been less studied. There are lots of evidences suggesting that various complications of preeclampsia, including vascular reactivity changes, vasospasm and multiorganic pathologies, occur due to the development of pathological changes in maternal vascular endothelium (Hung T. H. et al 2002, Redwan G.W.G. et. al. 2000, Hubel C. A. 1999). There has been suggested that nitric oxide deficiency plays significant role in the development of structural and functional changes of vascular endothelium in maternal organism (Hung T. H. et al. 2001).

Proceeding from aforesaid, our research aimed to study changes in placental NO levels during physiological pregnancy and pregnancy complicated with preeclampsia.

MATERIAL AND METHODS

Blood samples of 35 pregnant women with 24th-36th-week of gestation have been studied. Among them 19 women had physiological pregnancy (without complications) and 16 women - pregnancy complicated with preeclampsia. Preeclampsia has been diagnosed according to modern standards of classification (Clifford J. M. et.al, 2000). In particular, systolic arterial blood pressure on 20th week of gestation period was >140 mm g, diastolic - > 90 mm g. Proteinuria and edema have been detected.

In order to study nitric oxide metabolism in placenta, we measured the levels of free nitric oxide (NO) and NO complexes with hemoglobin. For the purpose of free nitric oxide determination in placenta we placed tissue samples in 1 molar solution of sodium diethyldithiocarbamate (SIGMA) for 30 minutes. EPR spectra have been determined on radio spectrometer RE-1307 (Russia) at the temperature of liquid nitrogen.

RESULTS AND DISCUSSION

The table shows changes in NO levels during physiological and pathological (complicated with preeclampsia) pregnancy. It appeared, that physiological pregnancy is characterized by approximately equal distribution of free NO content between maternal and fetal sides of placental tissue (see the table 1). At that, low intensity EPR signal of HBNO complexes was revealed in maternal side of placental tissue. During pregnancy complicated with preeclampsia free NO levels in placental tissue are drastically decreased, especially in maternal side. At the same time, EPR signal of HBNO complexes is revealed throughout the tissue and its intensity is drastically enhanced.

Insufficient invasion of extra lanate cytotrophoblastic cells into endometrium during the first trimester of pregnancy has been considered to be one of the preconditions for the development of preeclampsia (Drosans et al 1972). It results in incomplete reorganization of spiral arteries, that prevents dilation of myometrium segment. Consequently, these blood vessels are characterized by high resistance, which is associated with decreased uteroplacental perfusion (Mekings J.W. et al, 1986, AquilineJ, et al, 1996, Beinder E 1999). It has been suggested that high vasoreactivity of defective remodeled arteries causes a decrease in blood flow from maternal organism to lanate space (Hung T.H. et al, 2001). Under the conditions of vasoconstriction blood supply of placenta is decreased that results in hypoxia of fetus.

A number of studies (Labe J.A. 1999) demonstrated that iNOS gene mutations is one of risk factors for pregnant's preEclampsia. There has been revealed drastic decrease in placental lanate cell eNOS mRNA and inhibition of iNOS synthesis during preEclampsia (Tong X et al, 1998, Zhou R, et al, 1998).

	N	NO	HbNO
Blood from umbilical cord of women at timely physiological childbirth	10	58, 8± 8,3	12,3± 2,8
Blood from umbilical cord of women at child birth in case of pregnancy complicated with preeclampsia	8	26, 7± 5,4 p<0,001	26,1± 1,5 p<0,05

Tab.1 Changes in free NO levels during physiological and pathological (complicated with preeclampsia) pregnancies in placenta of women at childbirth.

CONCLUSION

In conclusion, as it proceeds from the analysis of literary data and the results obtained in our study, lowered free NO levels in placental tissue, detected by us during preeclampsia, may be due to eNOS gene mutation as well as to decreased expression of this enzyme and

inhibition of iNOS synthesis. At the same time, significant elevation of nitrosyled hemoglobin (HbNO) levels in placenta during preeclampsia indicates the development of tissue hypoxia. Enhanced generation of HbNO complexes results in restriction of NO physiological function, placental dysfunction and aggravation of fetoplacental circulation deficiency.

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Изменение содержания оксида азота в ткани плаценты при физиологическом и патологическом течении беременности

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Р Е З Ю М Е

Многочисленные факты свидетельствуют о важной роли оксида азота в регуляции фетоплацентарного кровообращения и сократительной активности матки при беременности и родах. Считают, что в патогенезе многочисленных осложнений преэклампсии значительная роль принадлежит нарушениям метаболизма оксида азота. В связи с этим целью нашего исследования явилось изучение изменений содержания свободного NO в плаценте при физиологическом и патологическом (осложненном преэклампсией) течении беременности. Установлено, что при беременности, осложненной преэклампсией, в плаценте содержание свободного оксида азота уменьшается, а концентрация нитрилизированного гемоглобина (комплексов HbNO) значительно увеличивается по отношению к их уровню у женщин с физиологическим течением беременности. Это обстоятельство, в первую очередь, указывает на подавление образования синтеза оксида азота в плаценте при преэклампсии. Повышение уровня нитрозогемоглобина (HbNO) свидетельствует о развитии гипоксии в ткани и, в свою очередь, обеспечивает снижение содержания свободного NO у беременных с преэклампсией, что способствует дальнейшему повышению резистентности кровеносных сосудов, усугублению эндотелиальной дисфункции и недостаточности фетоплацентарного кровообращения.

Ключевые слова: плацента, оксидационный стресс, окись азота, преэклампсия