

Changes in Free NO Levels in Umbilical Cord Blood of Women in Labor at Physiological Pregnancy and Pregnancy Complicated with Pre-eclampsia

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ABSTRACT

So far the etiology and pathogenesis of one of the frequent and dangerous complication of pregnancy, pre-eclampsia has been less studied. There are lots of evidences suggesting that various complications of pre-eclampsia, 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. Numerous evidences also prove a significant role of nitric oxide in regulation of uterine contractility during pregnancy and childbirth. Proceeding from aforesaid, our research aimed to study changes in blood NO levels of umbilical cord of women at childbirth during physiological pregnancy and pregnancy complicated with pre-eclampsia. As it proceeds from the results obtained in our study, in cases of pregnancy complicated with pre-eclampsia intensity of EPR signal of HbNO complexes in umbilical cord blood of women at childbirth is much higher as compared with those of women with physiological pregnancy. This fact first of all, indicates an activation of inducible NOS (iNOS) and enhanced generation of nitric oxide under the conditions of oxidative stress, characteristic of pre-eclampsia. Excessive NO easily nitrosylates deoxyhemoglobin with formation of nitrosohemoglobin (HbNO). This mechanism provides a decrease in free NO blood levels. Under the conditions of oxidative stress free nitric oxide may be also converted to cytotoxic peroxynitrite, which displays high constrictive activity. Significant lowering of free NO body levels during pregnancy complicated with pre-eclampsia contributes to the enhancement of vascular resistance and aggravation of endothelium dysfunction, characteristic of this syndrome, and may induce activation of uterine contractility and pathological childbirth.

KEYWORDS: *pregnancy, Umbilical Cord Blood, nitric oxide, pre-eclampsia*

So far the etiology and pathogenesis of one of the frequent and dangerous complication of pregnancy, pre-eclampsia has been less studied. There are lots of evidences suggesting that various complications of pre-eclampsia, 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). Numerous evidences also prove a significant role of nitric oxide in regulation of uterine contractility during pregnancy and childbirth.

Proceeding from aforesaid, our research aimed to study changes in blood NO levels of umbilical cord of women at childbirth during physiological pregnancy and pregnancy complicated with pre-eclampsia.

MATERIALS 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 pre-eclampsia. Pre-eclampsia 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.

DISCUSSION OF OBTAINED RESULTS

The table shows changes in free NO and HbNO blood levels in umbilical cord of women at childbirth during physiological pregnancy and pregnancy complicated with pre-eclampsia. During physiological pregnancy NO blood levels in umbilical cord of women at childbirth are slightly decreased as compared with those of healthy women. In women at childbirth during pregnancy complicated with pre-eclampsia NO blood levels in umbilical cord tend to decrease as compared with those of physiological pregnancy (see the table). here should be indicated also that during both physiological pregnancy and pregnancy complicated with pre-eclampsia EPR spectra of umbilical cord blood of examined women in labor reveal EPR signal of HbNO complexes. At that, during pregnancy complicated with pre-eclampsia these parameters are 26% higher as compared with those of physiological pregnancy.

In the course of physiological pregnancy augmentation of hormone - dependent synthesis of NO plays a significant role in maintenance of "physiological quiet" of uterus. NO affects smooth muscular system of uterus through the activation of guanilat cyclase. The latter results in decreased diacylation of arachidonic acid and lowered prostaglandin, leukotriene and endothelin synthesis (Khugashvili P, 2000). At timely physiological childbirth undesirable relaxing effect of NO is neutralized by nitrosylation of deoxyhemoglobin and formation of HbNO complexes under the condition of hypoxia, characteristic of childbirth process. EPR signals of HbNO complexes have been registered in blood of women in labor. (Khugashvili P, 2000).

	N	NO	HbNO
Blood of healthy non-pregnant women	25	16,0±1,5	-
Umbilical cord blood of women at timely physiological childbirth	19	13,8±1,6	14,0±1,5
Umbilical cord blood of women at childbirth during pregnancy complicated with pre-eclampsia	16	12,4±1,4	27,6±1,6

Tab.1 Changes in free NO blood levels during physiological and pathological (complicated with preeclampsy) pregnancies in umbilical cord of women at childbirth.

As it proceeds from the results obtained in our study, in cases of pregnancy complicated with pre-eclampsia

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Изменение содержания оксида азота в пуповинной крови рожениц с физиологическим и патологическим течением беременности

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РЕЗЮМЕ

Многочисленные факты свидетельствуют о важной роли оксида азота в регуляции сократительной активности матки во время беременности и родов. Считается, что в патогенезе многочисленных осложнений преэклампсии значительная роль принадлежит нарушениям метаболизма оксида азота. Целью исследования являлось изучение содержания свободного NO в пуповинной крови рожениц с физиологическим и патологическим, осложненным преэклампсией течением беременности. Установлено, что при беременности, осложненной преэклампсией, в пуповинной крови рожениц содержание свободного оксида азота уменьшается, а концентрация нитрозилированного гемоглобина (комплексов HbNO) значительно увеличивается в сравнении с их уровнем у женщин с физиологическим течением беременности. Это обстоятельство, в первую очередь, указывает на интенсификацию синтеза оксида азота индуцибельной NO-синтазой, усиленно экспрессируемой в условиях характерного для преэклампсии окислительного стресса. Избыточное NO нитрозилирует дезоксигемоглобин с образованием HbNO комплексов. Этот механизм обеспечивает в крови рожениц с преэклампсией снижение содержания свободного NO, что способствует характерному для этого синдрома повышению резистентности кровеносных сосудов и усугублению эндотелиальной дисфункции, а также способствует чрезмерной активации сократительной деятельности матки, что может стать причиной патологических родов.

КЛЮЧЕВЫЕ СЛОВА: беременность, пуповинная кровь, оксид азота, преэклампсия