Nitric oxide and lipid free radicals at neonatal bilirubinemia

Tea Abzhandadze, Avtandil Kvezereli-Kopadze, Ether Japaridze, Tamar Sanikidze

I. Pagava Pediatric Scientific Research Institute, Tbilisi, Georgia

ABSTRACT

The present work was aimed to investigate intensity of free radical oxidation in the blood of neonates with hyperbilirubinemia. Has been defined content of lipoperoxides and free nitric oxide in the blood of practically healthy newborns and newborns with hyperbilirubinemia using the electronic-paramagnetic resonance method (EPR) and corresponding spin traps - α-phenyl-*tert*-buthylnitron (PBN) and Na-diethyldithiocarbamat (DETC) (SIGMA). Results of carried out investigations have shown that in the blood of neonates with hyperbilirubinemia process of lipid peroxidation is intensified leading to the activation of inducible NO-synthase expression and production of nitric oxide in organism.

KEYWORDS: *nitric oxide, hyperbilirubinemia, neonates, free radicals, inducible NO-synthase*

Newborns' jaundice is the manifestation of hyperbilirubinemia that develops in neonatal period.

In newborn's organism developed hyperbilirubinemia is the result of hemoglobin, myoglobin and iron-containing proteins' exaggerated breakdown. Released bilirubin circulates in complex with albumin and releases from organism.

Unconjugated bilirubin goes through the blood-brain barrier and reveals toxic effect [1].

Numerous investigations confirm the fact about bilirubin's antioxidant properties and activity [4,6,7] however, its role in neonate's organism is not completely clear and stated [5].

Coming from the aforesaid the aim of our investigation is detection of intensity of oxidized metabolism and nitric oxide at newborns' hyperbilirubinemia.

MATERIAL AND METHOD

Has been studied the blood of 15 neonates. They were treated at I. Pagava Pediatric Scientific Research Institute. Practically healthy 8 neonates consisted the control group. Has been defined blood count, bilirubin level, lipoperoxidative free radicals and free nitric oxide (NO) content.

Blood lipoperoxidative free radicals' content (LOO.) has been defined by the electronic-paramagnetic resonance method (EPR) using the spin-trap - α-phenyl-*tert*-buthylnitron (PBN) (Sigma) with the dose of 150 mM/l PBN 2,5 mM/l tris-HCl in buffer - pH=7,4 [3].

LOO. EPR specters were registered on the radiospectrometer РЭ-1307 at room temperature. Microwave radiation - 20 mVt.

Free nitric oxide in blood has been defined using the spin-trap – Na-diethyldithiocarbamat (DETC) (SIGMA) with the dose of 500 mg/kg and Fe^{2+}-citrate (50 mg $FeSO_4^+$. $7H_2O$+37,5 mg Na- citrate kg^{-1}).

EPR specter of NO-Fe^{2+}-$(DETC)_2$ complexes has been defined at the temperature of liquid nitrogen and microwave radiation - 20 mVt [2].

RESULTS AND DISCUSSION

The table has shown lipids' free radicals (LOO.) and free nitric oxide content in newborns with hyperbilirubinemia.

	NO	LOO·
Control	16,0±0,8	-
Hyperbilirubinemia	22,0±1,2	8,7±1, 4

Tab.1 *Changes of lipids' free radicals (LOO.) and free nitric oxide content in newborns' blood.*

According to the obtained results, in case of hyperbilirubinemia in newborns' blood the lipids' free radicals (LOO.) and free nitric oxide content are increased.

EPR signal of spin-labeled lipoperoxides' in blood indicates high intensity of free radical oxidation processes.

Intensification of free radical oxidation and exaggerated production of reactive forms of oxygen support increased expression of inducible NO-synthase (iNOS) that is revealed by the sharp increase in nitric oxide concentration in blood.

Thus, proceeding from the results of our investigations could be concluded that in case of newborns hyperbilirubinemia the intensity of free radical oxidation processes and production of nitric oxide are increased.

REFERENCES:

1. Сутулина И.М. Желтухи у детей первых месяцев жизни. Мать и дитя в Кузбасе., 2003, 4, 11-15.
2. Галаган М.Е., Киладзе С.В. Ванин А.Ф. (1997) Биофизика, 3, 687-692.
3. Tabatabaie T., Vasquez-Weldon A., Moore D.R., Kotake Y. (1997) Diabetes., 52, 1994-1999.

4. Moller N.J., Rice-Evans C., Davies M.J., et al. A novel method for measuring antioxidant capacity and its application to monitoring the antioxidant status in premature neonates. Clin. Sci., 1993, 84, 407-412.

5. Dani C., Martelli E., Bertini G., Pezzati M., Filippi L., Rossetti M., Rizzuti G., Rubaltelli F.F. Plasma bilirubun level and oxidative stress in preterm infants. Arch. Did. Cgild Fetal Neonatal Ed., 2003, 88, 119-123

6. Stoker R., Ames B.N. Potential role of conjugated bilirubin and copper in the metabolism of lipid peroxides. Proc. Natl. Acad. Sci. USA., 1987, 69, 8130-8138.

7. Stoker R., Yamamoto Y., McDanogh A.F., et al. Bilirubin is an antioxidant of possible physiological impotance., Science., 1987, 235, 407-412.

Свободные радикалы липидов и оксида азота при гипербилирубинемии

Тея Абжандадзе, Автандил Квезерели-Копадзе, Этер Джапаридзе, Тамар Саникидзе

НИИ педиатрии им. И.Пагава, Тбилиси, Грузия

Р Е З Ю М Е

Целью работы являлось исследование интенсивности свободнорадикального окисления в крови младенцев с гипербилирубинемией. С помощью метода электронного парамагнитного резонанса (ЭПР) и применения соответствующих спин-меток α-фенил-tert-бутилнитрон (PBN) и диэтилдитиокарбамата натрия (DETC) (SIGMA) определяли содержание липопероксидов и свободного оксида азота в крови практически здоровых младенцев и новорожденных с гипербилирубинемией. Результаты исследования свидетельствует об интенсификации процессов липопероксидации в крови младенцев с гипербилирубинемией, что способствует активации экспрессии индуцибельной NO-синтазы и интенсификации образования оксида азота в организме.

Ключевые слова: *оксид азота, гипербилирубинемия, новорожденные, свободные радикалы, идуцибельная NO-синтаза*

□ **International committee of medical journal editors. Uniform requirements for manuscripts submitted to biomedical journals.** Ann Intern Med 1997;126:36–47.

●*Issues To Consider before Submitting a Manuscript*

Redundant or Duplicate Publication

Redundant or duplicate publication is publication of a paper that overlaps substantially with one already published.

Readers of primary source periodicals deserve to be able to trust that what they are reading is original unless there is a clear statement that the article is being republished by the choice of the author and editor. The bases of this position are international copyright laws, ethical conduct, and cost-effective use of resources.

Most journals do not wish to receive papers on work that has already been reported in large part in a published article or is contained in another paper that has been submitted or accepted for publication elsewhere, in print or in electronic media. This policy does not preclude the journal considering a paper that has been rejected by another journal, or a complete report that follows publication of a preliminary report, such as an abstract or poster displayed for colleagues at a professional meeting. Nor does it prevent journals considering a paper that has been presented at a scientific meeting but not published in full or that is being considered for publication in a proceedings or similar format. Press reports of scheduled meetings will not usually be regarded as breaches of this rule, but such reports should not be amplified by additional data or copies of tables and illustrations.

When submitting a paper, the author should always make a full statement to the editor about all submissions and previous reports that might be regarded as redundant or duplicate publication of the same or very similar work. The author should alert the editor if the work includes subjects about which a previous report has been published. Any such work should be referred to and referenced in the new paper. Copies of such material should be included with the submitted paper to help the editor decide how to handle the matter.

If redundant or duplicate publication is attempted or occurs without such notification, authors should expect editorial action to be taken. At the least, prompt rejection of the submitted manuscript should be expected. If the editor was not aware of the violations and the article has already been published, then a notice of redundant or duplicate publication will probably be published with or without the author's explanation or approval.

Preliminary release, usually to public media, of scientific information described in a paper that has been accepted but not yet published violates the policies of many journals. In a few cases, and only by arrangement with the editor, preliminary release of data may be acceptable-for example, if there is a public health emergency.

Acceptable Secondary Publication

Secondary publication in the same or another language, especially in other countries, is justifiable, and can be beneficial, provided all of the following conditions are met.

1. The authors have received approval from the editors of both journals; the editor concerned with secondary publication must have a photocopy, reprint, or manuscript of the primary version.

2. The priority of the primary publication is respected by a publication interval of at least one week (unless specifically negotiated otherwise by both editors).

3. The paper for secondary publication is intended for a different group of readers; an abbreviated version could be sufficient.

4. The secondary version faithfully reflects the data and interpretations of the primary version.