

Oxidative stress in respiratory failure in pediatric patients

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ABSTRACT

Acute respiratory failure is the frequent cause of patient admission to intensive care unit, or it is common complication of severe pathological conditions. Most patients with acute respiratory failure, who experience hypoxia, need supplemental oxygen in high concentrations. The goal of our research was to study the status of oxidative stress and efficiency of treatment with supplemental oxygen in pediatric patients with acute respiratory failure. The results of the research showed, that use of supplemental oxygen, especially in long-term treatment can aggravate oxidative stress with further damage to body tissues.

KEYWORDS: *oxidative stress, respiratory failure, hypoxia*

Consumption and metabolism of oxygen, which is "universal source" for aerobic organism is accompanied with undesirable effect-production of free radicals. Oxygen free radicals react with nucleic acids, proteins, fatty acids, cause peroxide acidification of lipids (PAL), change the structure of DNA, produce mutations with subsequent malignant growth. In the process of evolution biologic systems formed protective antioxidant mechanisms (Guest J.R. 1995) to keep the organism from damage. Thus, breathing of ambient air FiO_2 21% in normal oxygenation is followed by balance between formation and inactivation of free radicals, so called pro-antioxidative balance (Baines D.L, et al, 2001). In different situation-excessive amount of active forms of oxygen or deficiency of their inactivation can cause oxidative stress.

In most patients of Intensive Care Unit with respiratory failure, who experience hypoxia and need supplemental oxygen in high concentrations (FiO_2) we see excessive production of active forms of oxygen.

Nitric oxide (primary prooxidant) in normal situation is the agent which regulates the tone of the blood vessels. Hypoxic condition produce high amount of NO, which can cause relaxation of blood vessels and improvement of oxygen delivery to the body tissues. When the blood contains superoxidradical (reactive form of oxygen), which reacts with nitric oxide and produce peroxid nitrit with high level of toxicity, we see markedly increased constriction of blood vessels.

The goal of our research was to study the status of oxidative stress and efficiency of treatment with supplemental oxygen in patients with respiratory failure. Thus, we investigated production of active forms of nitrogen and oxygen in patients with acute respiratory failure in different stages of treatment with supplemental oxygen.

MATERIAL AND METHODS

We have investigated 45 pediatric patients (4-6 years old) with acute respiratory failure admitted to the Pediatric Intensive Care Unit of Tbilisi State Medical University Pediatric Clinic. Patients were divided to the groups according to the treatment with supplemental oxygen. Group I consisted of patients before treatment. Group II and group III contained patients during treatment with oxygen ($FiO_2 > 60\%$), with different duration from several (6) hours (group II) to several (4-6) days (group III). Oxygen was delivered in low (by face mask or nasal canula) or high flow by BiPAP method. Control consisted of 20 out-patients of the same age.

For the estimation of free radical forms of nitrogen and oxygen we used the method of an electro-paramagnetic resonance (EPR) which is based on the absorption of high frequency microwave radiation by paramagnetic particles. For the fixation of unstable molecules special labels were added to the blood. EPR signals of the blood samples were measured in radiospectrometer PE 1307.

RESULTS AND DISCUSSION

The table presents the changes in content of active forms of nitrogen and oxygen in the blood of critical patients before and during treatment with supplemental oxygen.

In the blood of control we didn't registrate an electro-paramagnetic resonance (EPR) signal of superoxid radicals.

In the blood of the patients with hypoxia (group I) before treatment with supplemental oxygen we revealed mild EPR signal of labeled superoxidradical, EPR signal of free nitric oxide was 30% higher than in control. We also registrated low EPR signals for HbNO and methemoglobin.

Appearance of superoxidradicals is the sign of increased production of them and deficiency of protective systems, as well as reduction in the affinity between hemoglobin and oxygen in respiratory acidosis and tissue hypoxia. It is important to emphasize, that high affinity of hemoglobin with nitric oxide in hypoxic conditions with low PO_2 cause the production of HbNO, which in presence of reactive oxygen create methemoglobin and nitrite (NO_2). (Gow A.J, Stamler J.S, 1998).

Thus, acute respiratory failure with hypoxia in children can cause increased production of NO, superoxid radicals, HbNO and methemoglobin, which can further aggravate hypoxia. Additionally, in hypoxic conditions formation of hypoxic-inductive factor (HIF-1 α) and redox-sensitive nuclear factor (NFkB) promotes the adaptation of the organism to hypoxia. (Haddad J.J, 2001).

The patient is not ready to breathe the oxygen in high concentration. Confirmation of this statement is extreme increase in the level of reactive forms of nitrogen and oxygen in blood. Intensity of the production of these substances is in deep correlation with the duration of treatment with supplemental oxygen. After 6 hours of treatment (group II) we revealed high EPR signal of labeled superoxidradical (100% elevation), as well as intensity of EPR signal of labeled nitric oxide was same as in control. In long-term treatment with supplemental oxygen (4-6 days, group III) we revealed increased EPR

signals of nitric oxide and oxygen free radicals (100%-130% elevation in difference with basic levels).

In the basis of above-mentioned, we can conclude, that treatment with supplemental oxygen can aggravate oxidative stress in patients with acute respiratory failure. Despite improvement of blood PO₂ level, first hours of treatment with oxygen reveal elevated content of HbNO,

which decreases oxygen-carrying capacity of the erythrocytes, oxygen supply to the body tissues and disturbs oxidation metabolism in tissues. Thus, it seems that most of supplemental oxygen is not delivered to the body and goes to free radical process. Both oxidative stress and hypoxic alterations result in secondary damage of cell membranes and irreversible disturbance of the human body.

Patient groups	Number of patients	O ₂ (mm/mg)	NO (mm/mg)	HbNO (mm/mg)	MetHb (mm/mg)
Control	20	-	10±0,9	-	-
I group (Before treatment)	13	5,0±1,0	13,5±1,0	6,3±0,9	4,5±0,5
II group (After 6 hours during treatment)	15	10,0±1,1	12,8±1,1	10,0±1,0	5,0 ±0,6
III group (After 4-6 days during treatment)	17	20,0±1,5	30,0±1,5	15,0±1,3	8,0±0,6

Tab.1 changes in content of active forms of nitrogen and oxygen in the blood of critical patients before and during treatment with supplemental oxygen.

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Окислительный стресс при острой дыхательной недостаточности у детей

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РЕЗЮМЕ

Обследовано 45 больных детей с острой дыхательной недостаточностью. Изучено содержание активных форм азота и кислорода в крови. Установлены параметры окислительного стресса. Предложены режимы оксигенотерапии в зависимости от тяжести дыхательной недостаточности.

Ключевые слова: окислительный стресс, дыхательная недостаточность, гипоксия, оксигенотерапия

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

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