

PROTECTION OF NEWBORN ORGANISM AGAINST EFFECT OF OXIDATIVE STRESS

Brucknerová I.¹, Benedeková M.¹, Pecháň I.², Franková E.¹, Ujházy E.³, Dubovický M.³

¹ 1st Department of Paediatrics, Medical School, Comenius University, Bratislava

² Slovak Institute of Cardiovascular Diseases, Bratislava

³ Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovak Republic

SUMMARY

Objective: The aim of the present study was to investigate influence of oxidative stress on newborn organism, in terms of the dynamics of malondialdehyde (MDA) concentration changes and of the activities of selected antioxidants in asphyxial newborns on the 1st and 5th day of life.

Method: In the group of 62 preterm and term asphyxial newborns, characterized by the presence of asphyxial criteria and admitted within 24 hours of life, the plasma concentration of MDA and level of total antioxidant status (TAS) were followed. **Results:** Dynamic changes of MDA signalized active process of lipoperoxidation (LP) and values of TAS were decreased in comparison with the capacity of adult patients.

Key words: asphyxia, newborn, total antioxidant system, malondialdehyde

Address for correspondence: I. Brucknerová, 1st Department of Paediatrics, Medical School, Comenius University, Limbová 1, 833 40, Bratislava, Slovak Republic. E-mail: exfadubm@savba.sk

INTRODUCTION

The influence of free radicals (FR) and their reactive metabolites in organism takes an important role in a pathogenesis of so called “FR diseases”. The source of FR can be the disease of mother accompanied with hypoxemia, atherosclerotic changes of vessels or the affection of fetus mostly by asphyxia.

Asphyxia is a condition in which newborn’s organism is exposed to insufficient oxygen concentration. After exhaustion of compensatory mechanisms, the changes in function of

cells, tissues, organs and systems occur. In a case of severe asphyxia a multi-organ dysfunction of organism and death of child was found to occur (1). If there is a dysbalance between production and capacity of TAS the influence of oxidative stress (OS) takes place (2). The spectrum of consequences of OS is multifactorial. In a process of LP an oxidative damage of polyunsaturated carboxylic acids can occur. The more unsaturated is the higher carboxylic acid, the more sensitive is to OS. The consequence of LP is a formation of hydroxyperoxids of lipids and a whole spectrum of secondary metabolites, aldehydes and

ketones. Among most important aldehydes belongs MDA. The organism is protected against influence of FR by TAS, which is formed by set of all endogenous and exogenous antioxidant substances (3).

The aim of the study was to determine the influence of oxidative stress on newborn's organism, to observe the dynamics of MDA concentration changes and to determine the activity of TAS in asphyxial newborns on the 1st and 5th day of life.

METHODS

The study base was constituted by 62 asphyxial patients (38 preterm newborns, birth weight $1,888 \pm 109.86$ g and 24 term ones, birth weight $2,752 \pm 144.5$ g) admitted within 24 hours of life. In both groups of newborns we took samples of venous blood on the 1st and 5th day of life in which we analyzed the plasma concentration of MDA and level of TAS. For the quantitative evaluation of LP we used the reaction of MDA with thiobarbituric acid in an acid solution with the formation of violet product, which was measured spectrophotometrically (532-535 nm). TAS was measured by method, part of which (Randox Ltd., England) is an artificial production of radicals in a tested biological material. For the statistical analysis ANOVA by Fisher's post hoc test was used, $p \leq 0.05$ was considered to be significant.

RESULTS

MDA levels were without statistical significance in both groups between the 1st and 5th day of life (Fig. 1). After detailed analysis, we found an increased MDA levels in 75% of preterm newborns on the 5th day of life, while in a second group it was only 45%. Values of TAS in both investigated groups on the 1st day of life were about 20% lower compared to the lower level of TAS's values for adults. On the 5th day of life the TAS activity in a group of preterm asphyxial newborns increased while in a second group the activity decreased. Statistical significance ($p \leq 0.05$) was found between both groups on the 5th day of life (Fig. 2).

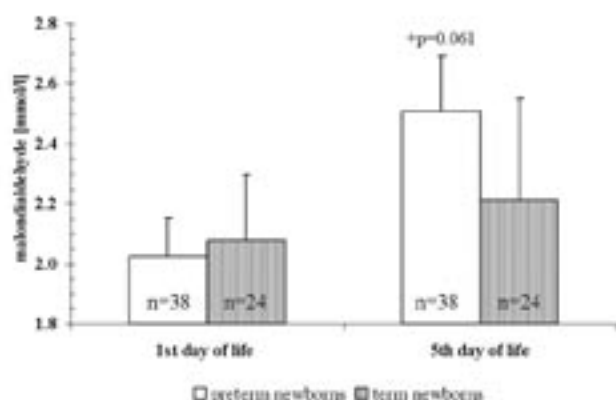


Fig. 1. Values of malondialdehyde in preterm and term asphyxial newborns. +p - marginal significance compared to preterm newborns on the 1st day of life (ANOVA).

DISCUSSION

The main source of LP during pregnancy is placenta (4, 5). We suppose that the rise of MDA levels in both groups is reflecting the presence of active process of LP, which was started by asphyxia and on the 5th day of life was supported by a presence at least of one of the risk factors (inhalation of O₂, lung ventilation, surfactant, transfusion of the erythrocyte mass, complete parenteral nutrition).

We assumed, that antioxidant potential by a healthy adequately weighted term newborn is high. It can be supported by the higher concentration of endogenous antioxidants (EA) like bilirubin (6). In a difference from our patients is the TAS expressively lower on the 1st day of life than in adults and higher levels of EA (total bilirubin, statistical significance $^{++}p \leq 0.01$, between the 1st and 5th day of life in both groups) did not compensate the higher production of FR formed in a process of LP. If the organism is pressed by eruption of sudden over-production of FR, it considerably exhausts its antioxidant capacity (7). The current values of TAS on the 5th day of life assumed stabilization of patient points on the ability of preterm asphyxial organism to increase the activity of TAS. We can presume the different level of ripe of chemical reactions according to gestational age. Also different intensity and length of asphyxia is important. If assumed, that organism of preterm newborn was prenatally longer under the influence of asphyxia (chronic asphyxia), it could increase the activity of TAS. The organism of term newborn was exposed to short asphyxia (acute asphyxia), which was probably so severe, that in order to overcome sudden OS it used all available amount of antioxidants. From the group of preterm asphyxial newborns 6 patients (16%) were delivered spontaneously and 32 patients (84%) were delivered by caesarian section. In the second group 19 newborns (79%) were delivered spontaneously and in 5 cases (21%) by caesarian section. The different entrance to life has also an influence on the origin of OS as it can make the asphyxia stronger (8).

In summary, the present study suggests that levels of MDA may be an useful indicator in a confirmation of a presence of active process of LP. The actual low levels of TAS on the 1st day of life can be a signal for supporting the ability of newborn's organism to cope better with the OS. Many questions about antioxidants remain unanswered, e.g. how could be the total antioxidant capacity

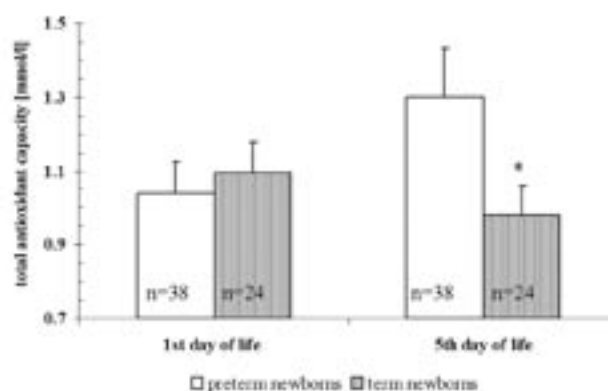


Fig. 2. Total antioxidant capacity in preterm and term asphyxial newborns. *p ≤ 0.05 - compared to preterm newborns on the 5th day of life (ANOVA).

of newborn's organism enhanced. Antioxidant supplementation was already attempted and proved beneficial in an animal experiment and in cardiovascular surgery (9-12).

REFERENCES

1. **Brucknerová I, Benedeková M:** Asphyxia of the newborn – the ever topical problem. *Biologia* 55/Suppl 2000; 8: 23-26.
2. **Toescu V, Nuttall SL, Martin U, Kendall MJ, Dunne F:** Oxidative stress and normal pregnancy. *Clin Endocrinol* 2002; 57: 609-613.
3. **Štípek S et al.:** Antioxidants and free radicals in health and disease development. GRADA publishing, 2000. (In Czech.)
4. **Mihailovic M, Cvetkovic M, Ljubic A, Kosanovic M, Nedeljkovic S, Jovanovic I, Pesut O:** Selenium and malondialdehyde content and glutathione peroxidase activity in maternal and umbilical cord blood and amniotic fluid. *Biol Trace Elem Res* 2000; 73: 1, 47-54.
5. **Steinerova A, Racek J, Stozicky F, Tatzber F, Lapin A:** Autoantibodies against oxidized LDL in the first phase of life. Low density lipoproteins. *Clin Chem Lab Med* 1999; 37: 913-917.
6. **Rickett GM, Kelly FJ:** Developmental expression of antioxidant enzymes in guinea-pig lung and liver. *Development* 1990; 108: 331-336.
7. **Ferrari R, Ceconi C, Curello S et al.:** Oxygen-mediated damage during ischemia and reperfusion: Role of the cellular defences against oxygen toxicity. *J Mol Cell Cardiol* 1985; 17: 937-945.
8. **Kaya H, Oral B, Ditttrich R, Ozkaya O:** Lipid peroxidation in umbilical arterial blood at birth: the effects of breech delivery. *BJOG* 2000; 107: 982-986.
9. **Ujházy E, Dubovický M, Faberová V, Zemánek M, Šoltés L, Gajdošík A, Eybl V:** Placental transfer of the antioxidant stobandine at different gestational stages in rabbits. *Method Find Exp Clin Pharmacol* 2000; 22: 638-688.
10. **Pecháň I, Holomáň M, Záhorec R, Rendeková V, Gabauer I:** Antioxidant vitamins and phosphocreatine as protective agents in cardiac surgery. *Biochemical parameters. Cor Europ* 1996; 5: 69-73.
11. **Holomáň M, Pecháň I:** The protection of myocardium in cardiovascular surgery. *ELÁN, Bratislava*, 2002.
12. **Holomáň M, Záhorec R, Rendeková V, Pecháň I:** Vitamin E for skeletal muscle protection against reperfusion injury during elective revascularization surgery (biochemical and clinical assessment). *Reprint Cor Vasa* 1999; 41: 73-83.