Superoxide Dismutase Activity in the Brain of Rats Prenatally Treated with Lead

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 128, No. 12, pp. 667-669, December, 1999
Original article submitted October 27, 1999

Cu/Zn superoxide dismutase activity in the brain of offspring of female rats treated with various concentrations of lead at various periods before and during pregnancy was reduced, which indicated disturbances of the antioxidant system.

Key Words: *lead; fetus; brain; superoxide dismutase*

Pathogenetic mechanisms underlying the effects of various pollutants on the body, especially at the early stages of embryogenesis are of considerable importance because of heavy environmental contamination. Lead is one of the most abundant toxicants [4]. Clinical and experimental studies demonstrated embryotoxic, teratogenic [1,2,8], and other adverse effects of lead and its salts on various organs and tissues of mammals [11,12].

Neurochemical mechanisms of the toxic effect of lead on the developing brain are still unclear. The analysis of effects of hazardous factors on developing brain indicates an important role of free-radical processes (FRP) in the pathogenesis of congenital cerebral disorders [5-7]. Impaired antioxidant mechanisms promote damaging effects of free radicals. Our previous studies revealed changes in activity of Cu/Zn superoxide dismutase (Cu/Zn-SOD), one of the major antioxidant enzymes, in the brain of rats prenatally exposed to various adverse factors [5,6].

The effects of prenatal exposure to lead on FRP and antioxidant enzyme activities in developing brain received little attention. These studies hold much promise for understanding of the pathogenetic mechanisms underlying the damaging effects of lead on fetus.

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Here we determined Cu/Zn-SOD activity in the brain of offspring of rats treated with various concentrations of lead at various periods before and during pregnancy.

MATERIALS AND METHODS

Experiments were performed on pregnant Wistar rats. The animals of groups 1 and 2 received lead nitrate (as the only source of water) in concentrations of 0.3 and 3.0 mg/liter, which 10- and 100-fold exceeded the maximum permissible concentrations (MPC), respectively. Each group was divided into 2 subgroups (a and b) receiving lead nitrate for 1 or 5 months before and during pregnancy, respectively. Control rats received distilled water.

All rats were decapitated on day 21 of pregnancy, the fetuses were rapidly removed, and the brains were isolated on ice, frozen, and kept at -42°C.

Whole brain preparations were obtained as described elsewhere [5]. SOD activity was assayed by inhibition of norepinephrine autooxidation in alkaline medium [13]. The enzyme concentration producing 50% inhibition of norepinephrine autooxidation was taken as a unit of activity. Protein concentration was measured by the method of Lowry. The results were analyzed by Student's *t* test.

RESULTS

SOD activities in the brain of fetuses from rats of groups 1a, 1b, 2a, and 2b were below the control by

0007-4888/99/0012-1239$22.00

29.5, 32.0, 21.2, and 39.4%, respectively (Table 1). There were no significant differences between experimental groups and subgroups in this parameter. However, it should be noted that brain SOD activity in fetuses from group 2b rats decreased to a greater extent (by 23%) compared to fetuses from group 2a rats.

Decreased SOD activity indicates dysfunction of the antioxidant system in the brain of fetuses prenatally exposed to lead, which can promote free radical-induced damage to the developing brain. It should be emphasized that lead in doses equal to 10 and 100 MPC caused practically similar damage to the brain.

Published data suggest that lead salts activate FRP in the blood, splenocytes, liver, and kidneys of adult animals [2,3]. Reduced SOD activity in the brain of fetuses is probably due to lead-induced damages to the enzyme molecule and its general toxic effects on the fetus and maternal body because of high permeability of the placental barrier for lead [12] and its accumulation in the embryo [1]. SOD can also be inhibited by high concentrations of free radicals and peroxides. In these experiments, the rats were treated with lead for 5 months before and during pregnancy and, therefore, fetuses developed under conditions promoting free radical generation and impaired antioxidant system.

There are data on high affinity of lead for membrane and mitochondrial cell structures. It damages cell structures [11] and disturbs respiration and oxidative phosphorylation in target organs [9,11]. These alterations in terminal oxidation lead to free radical overproduction [10]. Our previous experiments showed that prenatal exposure to ethanol impairs oxidative phosphorylation in the brain of offspring and decreases SOD activity [5]. The data suggest that enhanced production of free radicals depends on components of the respiratory chain during prenatal exposure to lead. After exhaustion of the antioxidant systems, FRP cause pathological changes in cells and their death [1,4].

Thus, decreased SOD activity after prenatal treatment with lead indicates considerable impairment of the antioxidant system in developing brain. These results confirm our hypothesis that FRP play an important role in the pathogenesis of prenatal disorders and should be taken into account when elaborating adequate methods for secondary prevention and correction of various disorders.

TABLE 1. Effect of Prenatal Exposure to Lead on SOD Activity in the Brain ($M \pm m$)

Group	Daily dose of lead, μg/kg	SOD activity, arb. units/mg protein
Control (n=8)		34.06±1.03
1a (n=8)	26.7	24.00±0.97**
1b (n=11)	26.6	23.23±0.47**
2a (n=6)	270.2	26.83±3.13*
2b (n=8)	250.3	20.64±1.75**

Note. *p<0.05 and **p<0.001 compared with the control.

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