Changes in the Antioxidant State and Intensity of Lipid Peroxidation in the Blood and Liver during 30-Day Hypokinesia

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 132, No. 10, pp. 387-389, October, 2001
Original article submitted January 31, 2001

Thirty-day hypokinesia was accompanied by an increase in plasma antioxidant activity and inactivation of liver antioxidant enzymes. The observed activation of blood antioxidant enzymes during hypokinesia was associated with increased resistance to acute hypoxic hypoxia.

Key Words: *hypokinesia; lipid peroxidation; antioxidant enzymes; hypoxia*

The resistance to acute hypoxic hypoxia is determined by activation of the antioxidant systems [7]. Stress and circulatory hypoxia accompanying long-term hypokinesia (HK) cause an imbalance between tissue and humoral antioxidant systems [2,7,8], which changes the content of lipid peroxidation (LPO) products in the blood and organs. The liver, the main source of lipoproteins accumulating LPO products, is of particular interest in this respect [12]. Peroxidized blood lipids are risk factors for polyorgan insufficiency and reduced hypoxia resistance [1,2]. Antioxidant factors (primarily ceruloplasmin and transferrin) preventing accumulation of LPO products are synthesized in the liver [14].

The relationship between antioxidant systems and intensity of LPO in the liver and blood during HK is poorly studied. The effects of long-term HK on organism's resistance to hypoxia remain unclear. This work was designed to solve these problems.

MATERIALS AND METHODS

Experiments were performed on 120 male and female albino Wistar rats. The animals were placed in tubes for 3, 7, 10, and 30 days for HK modeling and then sacrificed under light ether anesthesia. The content of LPO products in the plasma and liver was measured [3]. The content of primary (E_{232}/E_{220}) and secondary LPO products (E_{278}/E_{220}) in heptane (neutral lipids) and isopropanol (phospholipids) phases were estimated spectrophotometrically. Plasma antioxidant activity (AOA) was estimated by inhibition of peroxidation reaction in brain homogenates [3] and expressed in percents of the baseline. Catalase activity in liver homogenates was evaluated by H_2O_2 degradation [6,9]. Superoxide dismutase (SOD) activity was estimated by the inhibition of nitroblue tetrazolium reduction during non-enzymatic generation of superoxide radicals [11]. Animal sensitivity to hypoxia was estimated by the latency of hypoxic coma (sec) [3]. The results were analyzed by Student's t test, nonparametric Mann—Whitney U test, and exact Fischer's test.

RESULTS

During 30-day HK, the increase in blood AOA was accompanied by inactivation of SOD and catalase in the liver (Table 1). Despite the imbalance between humoral and tissue antioxidant factors, the content of LPO products in the blood and liver underwent similar changes. The concentrations of primary and secondary isopropanol-soluble LPO products in the plasma decreased on day 7 of HK. LPO in the liver was inhibited after 10-day HK, which was manifested in decreased content of primary heptane-soluble LPO products. The

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0007-4888/01/1324-0943$25.00

TABLE 1. Effect of Hypokinesia (30 Day) on LPO Intensity and Antioxidant System in the Blood and Liver ($M \pm m$)

Parameter	Hypokinesia, days			
	3	7	10	30
Latency of hypoxic coma, sec	85.09±4.12 / 89.00±2.46^{+}	83.25±2.95 / 92.25±2.50	82.00±2.07 / 82.50±4.15	82.00±2.07 / 91.2±3.0***
Blood				
AOA, %	25.45±1.40 / 29.32±1.31^{ooo}	26.03±1.25 / 29.50±1.02^{ooo}	27.31±1.47 / 27.34±2.31	19.0±2.6 / 36.26±5.27^{o}
LPO products (isopropanol phase)				
primary, E_{232}/E_{220}	0.516±0.139 / 0.507±0.120	0.529±0.023 / 0.346±0.062^{oo}	0.544±0.043 / 0.548±0.032	0.654±0.118 / 0.707±0.105
secondary, E_{278}/E_{220}	0.285±0.079 / 0.282±0.070	0.301±0.038 / 0.261±0.043^{oo}	0.331±0.038 / 0.327±0.027	0.318±0.084 / 0.383±0.111^{+}
Liver				
SOD, arb. U	0.91±0.004 / 0.91±0.08	0.910±0.004 / 0.870±0.006**	0.910±0.004 / 0.770±0.006*	1.03±0.04 / 0.890±0.0.008*
Catalase, nmol/mg protein/min	622.04±3.22 / 483.10±5.02*	622.04±3.22 / 441.87±2.12*	622.04±3.22 / 436.86±1.00*	268.50±4.46 / 245.70±3.44**
LPO products (heptane phase)				
primary, E_{232}/E_{220}	1.134±0.397 / 0.896±0.475	0.563±0.064 / 0.560±0.075	0.849±0.028 / 0.788±0.010^{ooo}	0.774±0.042 / 0.856±0.060^{oo}
secondary, E_{278}/E_{220}	1.190±0.161 / 0.808±0.333	0.226±0.069 / 0.260±0.063	0.324±0.021 / 0.287±0.041	0.514±0.25 / 0.567±0.190

Note. Numerator: control; denominator: hypokinesia. Significant difference from the control: *$p<0.001$, **$p<0.01$, and ***$p<0.05$, Student's t test; $^{+}p<0.05$, exact Fischer's test; $^{o}p<0.001$, $^{oo}p<0.01$, and $^{ooo}p<0.05$, Mann—Whitney test.

increase in AOA at the initial stage of HK was probably associated with not only the decrease in the content of circulating LPO products, but also inhibition of LPO in the liver. AOA considerably increased after 30-day HK. This was accompanied by intensification of LPO not only in the liver, but also in the plasma (as estimated by the contents of primary heptane-soluble and secondary isopropanol-soluble LPO products, respectively, Table 1). It should be emphasized that the appearance of hyperoxidized phospholipids in the plasma results from not only LPO activation in circulating lipoproteins, but also their migration from various organs (*e.g.*, liver) into the circulation [2]. These LPO products promote the development of neurocirculatory disorders and decrease the resistance to hypoxia [2,12,13]. However, accumulation of lipid peroxides in the blood after 30-day HK was associated with longer latency of hypoxic coma (Table 1). Moreover, AOA and resistance to hypoxia underwent parallel changes at various stages of HK. These data indicate that the contribution of various antioxidant factors, including ceruloplasmin, to potentiation of hypoxia resistance should be taken into account [5]. Since hypoxia is a general pathological process, we hypothesize that the increase in AOA during HK is an adaptive reaction. Previous studies showed that plasma AOA depends on protein-synthesizing function of the liver [14]. Probably, intensive secretion of humoral antioxidants suppresses synthesis of antioxidant enzymes from amino acids in hepatocytes. The increase in blood AOA is a component of the antihypoxic protection that involves various stress-limiting systems. Their role in the resistance to hypoxia during long-term HK should be studied in details.

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