

# Effects of Diuretics on the Intensity of Lipid Peroxidation and Antioxidant Protection of Blood Plasma

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An increase in the content of primary and final lipid peroxidation (LPO) products and a decrease in the fat- and water-soluble antioxidants in blood plasma are revealed in a study of hypohydration induced by administration of 40 mg furosemide alone or in combination with 1 tablet of triampur. Intensification of free radical processes in states simulating weightlessness may be related to the loss of fluid due to transformation of water-electrolyte metabolism.

**Key Words:** *lipid peroxidation; diene conjugates; malonic dialdehyde; antioxidant activity; vitamin E*

It is known that the transfer to weightlessness or to states modeling it is accompanied by redistribution of circulating blood. This leads to a decrease in the content of antidiuretic hormone and aldosterone production, which results in the loss of water, sodium, and potassium [7]. Therefore, medicamentous hypohydration to a certain degree can be regarded as a model of transformation of the water-electrolyte metabolism, one of the manifestations of weightlessness.

The results of experiments modeling weightlessness in animals and humans and short-term space flights testify to the activation of LPO in various tissues [5,10].

During the early period of immersion there is a concomitant increase in free radical oxidation and antioxidant protection. Later on, the antioxidant systems become depleted. This causes oxygen to exhibit toxic properties at its normal partial pressure in tissues [6]. LPO reactions play a very

important role in the transformation of the membrane structures [3].

So far, no evidence on the activity of the peroxidation processes during hypohydration has been obtained in modeling experiments or when the different effects of weightlessness have been analyzed.

The aim of this work was to study the activity of LPO and antioxidant protection of blood plasma during medicamentous hypohydration.

## MATERIALS AND METHODS

Seven essentially healthy male volunteers aged  $38.1 \pm 1.7$  years were enrolled in the study. Six of them participated in such studies two times. Blood was collected from the cubital vein using sodium citrate as an anticoagulant prior to and 4 h after the administration of the diuretic. The individuals were administered 40 mg furosemide (subgroup 1,  $n=13$ ) or 40 mg furosemide + 1 tablet triampur (subgroup 2,  $n=13$ ). The interval between the administration of these preparations was not less than 5 days.

The content of diene conjugates (DC) [3], malonic dialdehyde (MDA) [11], vitamin E [13]

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with modifications, and the total antioxidant activity (AOA) [9] with modifications were determined in the plasma obtained after centrifugation (1000 g, 15 min). Since DC and vitamin E are fat-soluble compounds, their levels were presented taking into account the plasma concentration of neutral lipids.

## RESULTS

A pronounced rise of primary and secondary LPO products occurred in both subgroups (Fig. 1). The DC content in subgroup 1 increased from  $1.39 \pm 0.08$  to  $1.80 \pm 0.09$   $\mu\text{M}/\text{mg}$  lipids and in subgroup 2 from  $1.33 \pm 0.06$  to  $1.66 \pm 0.11$   $\mu\text{M}/\text{mg}$  lipids.

The MDA content increased from  $4.53 \pm 0.65$  to  $7.14 \pm 0.97$  nM in subgroup 1 and from  $3.9 \pm 0.46$  to  $6.34 \pm 0.58$  nM plasma in subgroup 2.

In contrast to the increase in the peroxidation products, AOA dropped from  $8.4 \pm 2.5$  to  $4.5 \pm 1.0$  arbitrary units in subgroup 1 and from  $6.6 \pm 2.0$  to  $6.1 \pm 0.6$  arb. units in subgroup 2. The content of the major fat-soluble blood plasma antioxidant vitamin E [12] also decreased: in subgroup 1 from  $5.4 \pm 0.16$  to  $4.8 \pm 0.18$   $\mu\text{M}/\text{mg}$  lipids and in subgroup 2 from  $5.1 \pm 0.17$  to  $4.9 \pm 0.21$   $\mu\text{M}/\text{mg}$  (Fig. 1).

Thus, a statistically significant increase in DC and MDA together with the decrease in the content of vitamin E and AOA of the plasma testify to the accumulation of LPO products accompanied by depletion of fat- and water-soluble plasma antioxidants 4 h after the administration of furosemide alone or furosemide in combination with triampur.

The possibility of a change in the concentration of LPO products as a result of fluid loss is excluded by normalization of the fat-soluble compounds DC and vitamin E to the lipid content in the plasma samples.

The intensification of peroxidation processes observed in states simulating weightlessness [1] may be associated with hypohydration.

Activation of LPO processes after administration of diuretics should be taken into account not only in space medicine but also in clinical practice, for example, in circulatory insufficiency and hypertension, when there is an imbalance between peroxidation and antioxidant reactions [2,8], and diuretics are administered against this background.

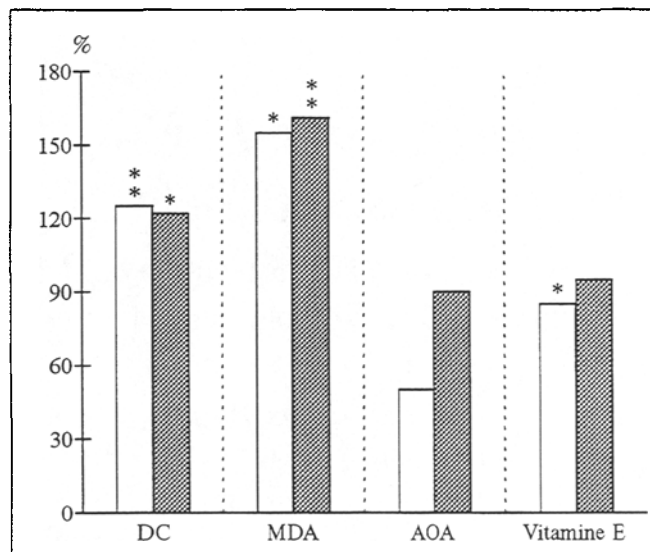


Fig. 1. Changes in the activity of peroxidation and antioxidant protection of blood plasma for medicamentous hypohydration. White bars: subgroup 1; black bars: subgroup 2. One asterisk indicates  $p < 0.05$ , two asterisks indicate  $p < 0.01$  compared with the corresponding background.

Therefore, in these cases administration of diuretics together with antioxidants is recommended.

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