Selenium Content and Blood Antioxidant Activity in Rats with Hereditary Arterial Hypertension during Experimental Myocardial Infarction

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The dynamics of selenium content in the plasma, lymph, and myocardium and plasma antioxidant activity were studied in male NISAG (hereditary stress-induced arterial hypertension) and Wistar rats with acute myocardial infarction and during recovery.In NISAG rats the decrease in selenium content correlated with the decrease in antioxidant activity. This probably aggravates the symptoms of experimental myocardial infarction in animals with hereditary arterial hypertension.

Key Words: *trace elements; arterial hypertension; myocardial infarction*

Studies of the pathogenesis and etiology of arterial hypertension and myocardial infarction opened many new aspects in these problems. It was established that trace elements, in particular, iron, copper, zinc, manganese, and selenium, essential components of enzymes systems, can affect the course of arterial hypertension and myocardial infarction. These trace elements modulate functions of pro- and antioxidant systems [5,12]. Metabolism of trace elements (*e.g.*, selenium) during ischemic injuries to the heart against the background of hereditary arterial hypertension is little studied [4].

Intensive production of reactive oxygen metabolites and activation of lipid peroxidation (LPO) are the main mechanisms underlying myocardial damages. Trace elements are the components of pro- and antioxidant systems. Taking into account these data, it is interesting to study blood antioxidant activity (AOA) in the dynamics of myocardial infarction. Here we studied the dynamics of selenium content in the plasma, lymph, and myocardium in normo- and hypertensive rats with experimental myocardial infarction (EMI) and evaluated the relationship between selenium concentration and AOA.

MATERIALS AND METHODS

Experiments were performed on 116 male normotensive Wistar and NISAG rats with hereditary stress-induced arterial hypertension (Institute of Cytology and Genetics). Blood pressure (BP) in these rats measured during stress was 205±2 mm Hg and the baseline BP was 170±2 mm Hg. The animals weighed 180-200 g. EMI was induced by subcutaneous injection of 0.1% epinephrine (0.2 mg/100 g) and verified electrocardiographically. The rats were decapitated under ether narcosis 1, 2, 3, 7, 14, and 21 days after epinephrine administration, and the blood was collected. Selenium content in the plasma, lymph, and myocardium was measured on an Unicum-939 atomic absorption spectrophotometer. Blood AOA was estimated by the chemiluminescence method. The plasma/lymph index (PLI) for selenium was calculated as the ratio between selenium contents in the plasma and lymph.

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RESULTS

Selenium contents in the plasma, lymph, and myocardium in control NISAG rats were higher than in normotensive animals (Fig. 1, *a*-*c*). This was probably related to pronounced antioxidant properties of selenium and more intensive functioning of antioxidant systems, which is confirmed by higher AOA activity in intact NISAG rats compared to Wistars (Fig. 1, *d*). Moreover, selenium produces a hypotensive effect [7,10], whose mechanisms are now intensively studied [8]. It can not be excluded that the increase in selenium content is associated with its involvement in the synthesis of triiodothyronine: conversion of thyroxin into triiodothyronine in the liver, kidneys, and thyroid gland is catalyzed by a selenium-containing enzyme [11]. Previous studies showed increased content of thyroid hormones in NISAG rats [1]. Thus, increased blood concentration of thyroid hormones can be a manifestation of adaptive processes in intact hypertensive animals, which confirms an important role of selenium in the regulation of systemic BP. However, this system functions on the verge of breakup, particularly, in the acute period of EIM. During this period selenium contents in the plasma and myocardium decreased in NISAG, but increased in Wistar rats. It was found that low selenium concentration is not only a risk factor for arterial hypertension [9] and myocardial infarction [6], but also a factor aggravating symptoms of myocardial ischemia [12]. Selenium plays an important role during EIM. This element is a component antioxidant enzymes (primarily, glutathione peroxidase, GSH-Px). GSH-Px is a homotetrameric selenium-containing protein protecting cells from ac-

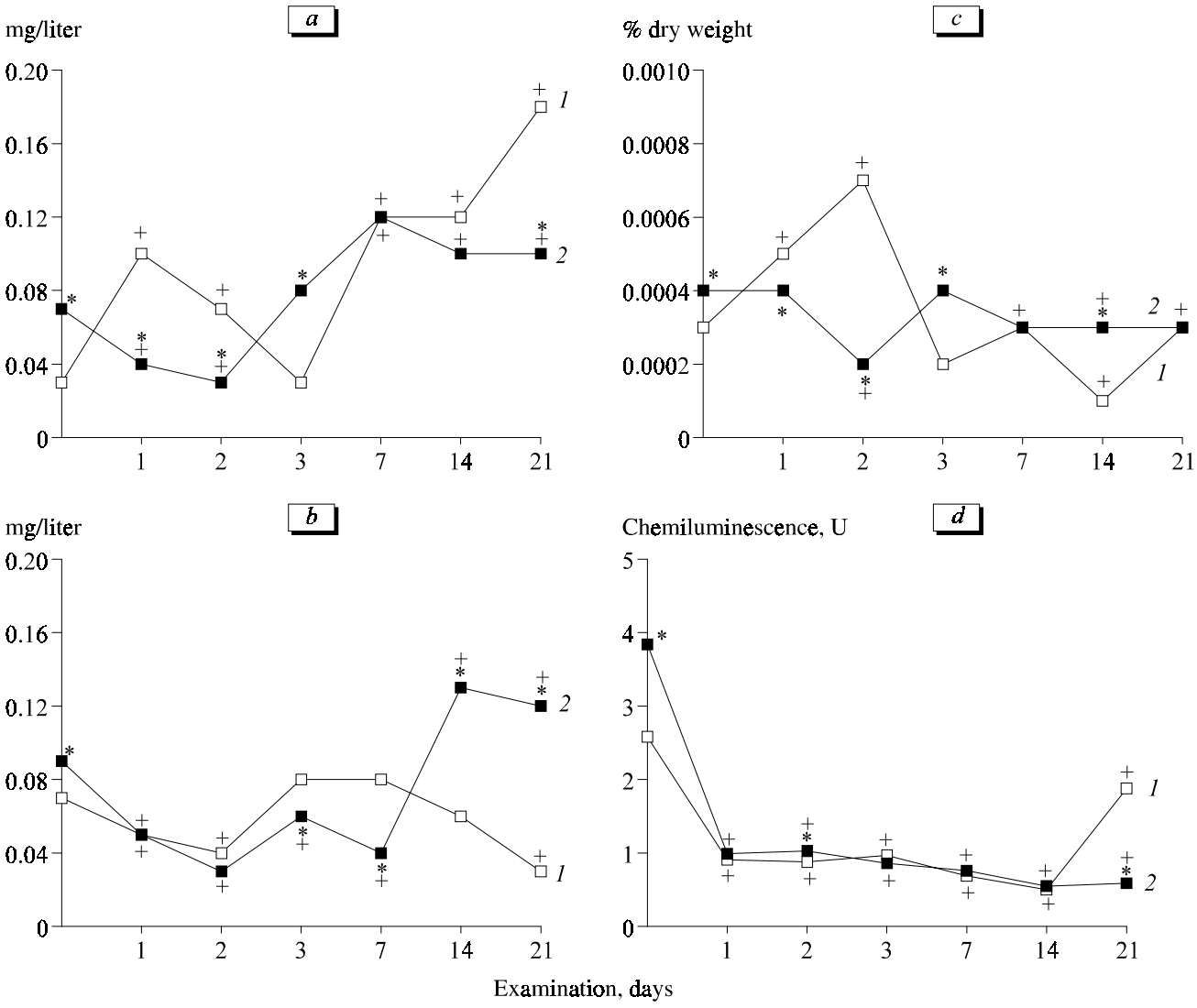

Fig. 1. Selenium content in the plasma (*a*), lymph (*b*), and myocardium (*c*) and plasma AOA (*d*) in Wistar (*1*) and NISAG rats (*2*) with experimental myocardial infarction. $p<0.05$: *compared to Wistar rats; +compared to the control (zero point on the abscissa).

cumulation of toxic hydroperoxides and free radicals. Selenium is integrated into GSH-Px in the form of selenomethionine during translation. Another selenium-containing enzyme phospholipid hydroperoxide glutathione peroxidase catalyzes reduction of hydroxyderivatives, in particular, phospholipid and cholesterol hydroperoxides, in the lipid phase of cell membranes and inhibits LPO in cells. A selenium-containing peptide possessing antioxidant properties and catalyzing the indirect degradation of superoxide radicals was isolated from rat myocardium. Moreover, selenium promotes production of endogenous protein and lipid antioxidants. It should be emphasized that selenium-containing amino acids produce antioxidant effects, since they scavenge free radicals and are involved in non-radical degradation of lipid peroxides [2]. Selenium attenuates cell damages during EIM, stimulates production of endogenous antioxidants, and, therefore, acts as a potent cardioprotector. Selenium-containing enzyme GSH-Px suppresses the synthesis of inflammatory mediators leukotrienes. This effects is realized via 2 pathways: first, inhibition of 5-lipoxygenase due to metabolism of its activators (fatty acid peroxides) and production of enzyme inhibitors (hydroxyacids), and second, competition for the substrate arachidonate-5-OOH. Thus, selenium acts as an inhibitor of leukotrienes and reduces the severity of inflammation during myocardial infarction.

Decreased concentration of selenium in the plasma, lymph, and myocardium in acute EMI, as well as low selenium content in the myocardium and a slight increase in plasma selenium content in NISAG rats during recovery are unfavorable factors aggravating the course of EMI (Fig. 1, *a-c*). In normotensive rats, the increase in plasma selenium content on days 14 and 21 positively correlated with normalization of AOA. A moderate correlation was found between selenium content and AOA in NISAG rats on day 21 after EMI modeling, which probably contributes to the absence of positive changes in plasma AOA during this period. On day 21 selenium PLI in Wistar rats increased by 14 times, which attested to redistribution of this element. However, on days 14 and 21 selenium PLI in NISAG rats did not differ from the control. This finding is of interest, since the plasma-lymph distribution of selenium is normalized at other concentrations of this element in the lymph and plasma.

These differences in selenium metabolism between NISAG and Wistar rats probably determines a more severe course of EMI in hypertensive animals. NISAG rats are characterized by a higher mortality rate and pronounced morphological and electrocardiographic signs of myocardial damages compared to normotensive animals [3]. Probably, disturbances in selenium metabolism aggravate the symptoms of EMI. The observed changes in selenium content can be related to genetically determined peculiarities (primary microelementosis) and EIM-induced disturbances in selenium metabolism (secondary postinfarction microelementosis) more pronounced in hypertensive rats. The observed relationship between selenium content, AOA, and severity of oxidative stress suggests that disturbances in the metabolism of trace elements (*e.g.*, selenium) play an important role in the pathogenesis of catecholamine-induced myocardial damages.

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