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EFFECT OF LEVAMISOLE (DECARIS) AND SODIUM NUCLEATE ON THE BLOOD ANTIOXIDATIVE SYSTEM OF GUINEA PIGS INHALING PAPRIN

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One of the causes of the decrease in nonspecific resistance of a patient requiring immunocorrection may be long exposure to products of microbiological synthesis and, in particular, paprin [1]. An important role in the mechanism of action of stimulators of immunity is played by activation of phagocytosis. It has been shown, in particular, the decaris and sodium nucleate can increase the phagocytic activity of macrophages and can also stimulate for formation of oxygen radicals by phagocytes [4, 6]. However, excessive production of oxidizing agents may lead to death of the phagocytic cell and to damage to surrounding tissues [8]. It is accordingly interesting to study the state of the antioxidative system (AOS) during administration of immunostimulators, for it protects cellular structures against the damaging action of oxidizing agents and free radicals and is an important component of the mechanisms of nonspecific resistance [11].

The aim of this investigation was to study the effect of decaris and sodium nucleate on the state of the OAS: the thiol-disulfide balance (SH/S-S) of the blood, lipid peroxidation (LPO), the plasma superoxide dismutase (SOD) activity, and glucose-6-phosphate dehydrogenase (G6PDH) and catalase activity of the erythrocytes, on a model of inhalation of paprin.

EXPERIMENTAL METHOD

Experiments were carried out on mature male guinea pigs weighing 250-300 g. All the animals were divided into four groups with eight individuals in each group: intact animals and three experimental groups. The experimental animals were placed in poisoning chambers where they inhaled paprin in a concentration of 3 mg/m^3 for 4 weeks, 4 h a day, 5 days a week; the intact animals were placed in similar chambers, ventilated with pure air. The experimental animals of the control group did not receive immunostimulators.

Animals of group 2 were given levamisole (decaris, from Gedeon Richter A. O., Hungary) in accordance with the following schedule: 2.5 mg/kg in 0.15 M NaCl solution, subcutaneously,

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TABLE 1. State of Blood AOS and LPO in Guinea Pigs Receiving Levamisole and Sodium Nucleate, and Inhaling Paprin (M ± m)

Parameter	Intact animals	Experimental animals		
		1 control	2-levamisole	3 sodium nucleate
Protein SH/S-S ratio (low-molecular weight	6,00±0,57	5,33±0,46	5,37±1,54	7,32±1,52
	4,29±1,99	5,76±1,09	5,86±1,41	4,64±0,66
G6PDH of erythrocytes, μmoles/g protein/sec	72,6±6,3	77,7±10,0	71,0±7,5	94,2±12,0
Erythrocytic catalase, nmoles/g protein/sec	29,04±3,0	42,67±7,7	49,6±7,4*	24,50±3,00**
Plasma SOD, % of inhibition	66,56±2,24	69,17±3,46	67,5±6,32	64,23±12,82
Plasma LPO, μmoles/MDA/liter	496±39	779±67*	911±96*	685±42**

Legend. Asterisk indicates significant difference from control; two asterisks — significant differences compared with group 2.

TABLE 2. Value of Coefficient of Correlation (ρ_s) between Parameters of Blood AOS in Guinea Pigs Exposed to Paprin and Immunostimulators

Parameter	Intact animals	Experimental animals		
		1 control	2 levamisole	3 sodium nucleate
Protein SH/S-S-low molecular-weight SH/S-S	+0,80	H_o	H_o	H_o
G6PDH-protein SH/S-S	H_o	H_o	−0,77	−1,00
G6PDH-SOD	H_o	H_o	−0,80	−1,00
G6PDH-catalase	+0,86	H_o	−1,00	+0,95
G6PDH-LPO	−0,80	H_o	+0,70	H_o

Legend. H_0) Null hypothesis.

two courses each of 3 days, separated by an interval of 5 days [6]. Animals of group 3 received sodium nucleate (USSR) in accordance with the schedule: 11 mg/kg in 0.25 M NaCl solution, subcutaneously, two courses each of 3 days, separated by an interval of 3 days [3]. Animals of group 1 received a 0.15 M solution of NaCl at the same times. Administration of the immunostimulators ended 2 days before the beginning of inhalation. Concentrations of SH- and S-S-groups were determined by reversed amperometric titration [9] in protein and nonprotein fractions of blood, after which the ratio SH/S-S was calculated, to reflect the trend of changes in the redox state of the system. The intensity of LPO was estimated by the malonic dialdehyde (MDA) concentration [2]. Activity of G6PDH, SOD, and catalase was determined by the methods in [5, 13, 15] respectively; protein was determined by Student's test; correlation was evaluated by Spearman's coefficient (ρ_s) [12].

EXPERIMENTAL RESULTS

The experimental animals of groups 1 and 2 showed a tendency for the value of the SH/S-S protein ratio to fall, whereas in the animals of group 3, it had a tendency to rise; the opposite tendencies were observed in the nonprotein fraction of the blood (Table 1). The opposite nature of changes in the redox state in the protein and low-molecular-weight thiols in the blood of the experimental animals led to a disturbance of correlation between then (Table 2). Considering the important role of thiol-disulfide interactions in regulation of protein conformation and function [10, 14], it is interesting to compare the data given above with values of activity of enzymes of the AOS and the intensity of LPO. Activity of erythrocytic enzymes and plasma SOD of the blood in control animals showed a tendency to rise, and the concentration of LPO products increased. In the animals of group 2, receiving levamisole, blood catalase activity was increased and LPO activity rose by an even greater degree than in group 1. In the animals receiving sodium nucleate, catalase activity of the

erythrocytes and the plasma MDA concentration were lower than in the previous group, whereas activity of G6PDH showed a tendency to rise and SOD activity a tendency to fall. The immunostimulators also had an effect on correlations betwen components of AOS and LPO. For instance, under the influence of levamisole and sodium nucleate, opposite relations develop between G6PDH activity, on the one hand, and the protein SH/S-S ratio and SOD activity, on the other hand (Table 2). Levamisole also inverted the G6PDH/catalase and G6PDH/LPO ratios. Positive correlation between G6PDH and catalase, characteristic of intact guinea pigs, persisted in the animals receiving sodium nucleate.

Thus levamisole was shown to have a pro-oxidant action. Both stimulators are able to change the correlation betwen parameters of AOS and LPO, but levamisole more so. It is evident that when a method of immunocorrection is being chosen, attention must be paid to the state of the AOS of the recipient and differences in the mechanisms of action of immunostimulators.

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