EFFECT OF THYMECTOMY AND THYMOSIN ON LIPID PEROXIDATION IN LYMPHOCYTES AND SUBCELLULAR HEPATIC ORGANELLES IN RATS

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Interaction between the neuroendocrine and thymicolymphatic systems, under hypothalamic control, is the basis of homeostasis, and disturbance of this interaction is the cause of many pathological processes and diseases [6, 7, 8, 10]. The main functions of the thymus, namely lymphopoietic, immunoregulatory, and endocrine are known but its influence on physiological and biochemical processes has not been finally established. In the last decades, studies of the role of the thymus in metabolism and energy in various organs and systems of the body have been published. The study of metabolic processes in organs and cells of the immune system and the subcellular structures of the liver is particularly interesting, for thymic hormone deficiency in immunodeficiency states leads in particular to changes in their struc tural and functional state.

To study the role of thymic hormones in the regulation of lipid peroxidation, we studied the effect of thymosin V on the concentration of malonic dialdehyde (MDA) in the course of spontaneous and ascorbate- and NADPH-dependent LPO in peripheral blood lymphocytes and subcellular hepatic organelles (mitochondria and microsomes) of thymectomized rats at different times after the operation (on the 40th, 70th, 100th, 190th, and 270th days).

EXPERIMENTAL METHOD

Noninbred male rats weighing 120-150 g were used. The animals were divided into three groups: I) rats undergoing a mock operation (control), II) thymectomized rats, and III) thymectomized rats receiving thymosin. Thymectomy was performed under ether anesthesia and with aseptic precautions [2]. The completeness of thymectomy was verified macroscopically at the time of the animals' death and also indirectly by the study of the leukocytic formula at intervals after the operation. Thymosin was injected intramuscularly into the thymectomized animals 1, 2, 3, 6, and 12 months after the operation for 10 days in a dose of 0.5 μg/g body weight daily. Control animals received injections of 0.85% sodium chloride solution on a similar schedule. The 5th fraction of thymosin, obtained by the method of Goldstein et al. [12], was used. Mitochondria were isolated from the liver by centrifugation of the supernatant fraction in 0.25 M sucrose [11]. The microsomal fraction of the liver was obtained by differential centrifugation on a VAC-601 centrifuge at 150,000g for 60 min [3]. Lymphocytes were isolated from peripheral blood on a Ficoll–Verografin gradient [9]. MDA was determined quantitatively by the method described by Vladimirov and Archakov [1]. The velocity of peroxidation was expressed in nmoles/mg protein. A molar extinction coefficient of $1.5 \cdot 10^5$ $m^{-1} \cdot cm^{-1}$ was used for the calculations.

EXPERIMENTAL RESULTS

The results of the study of the effect of thymectomy and thymosin on the intensity of phospholipid peroxidation in the liver mitochondria and microsomes and in peripheral blood lymphocytes are given in Figs. 1-3. They show that at different times

*Deceased.

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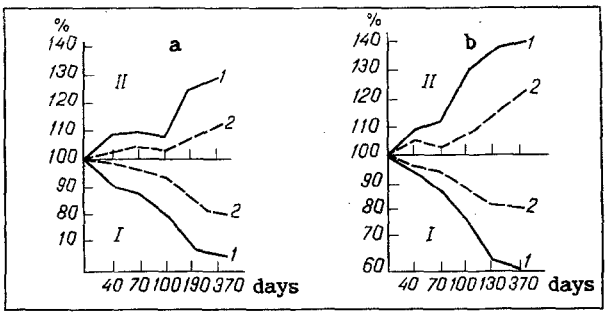

Fig. 1. MDA concentration in liver mitochondria (a) and peripheral blood lymphocytes (b) during spontaneous (I) and ascorbate-dependent (II) LPO. Here and in Figs. 2 and 3: abscissa, days of investigation; ordinate, MDA concentration (in % of control). 1) Thymectomized rats, 2) thymectomized rats receiving thymosin. Values differing statistically significantly from the control indicated by asterisk ($p < 0.05$-0.01).

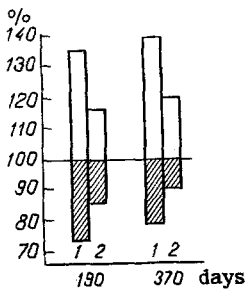

Fig. 2

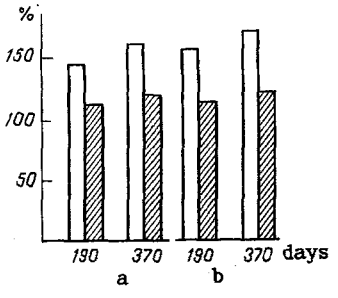

Fig. 3

Fig. 2. MDA concentration in rat liver microsomes during spontaneous (I) and ascorbate-dependent (II) LPO.

Fig. 3. MDA concentration in liver microsomes (a) and peripheral blood lymphocytes (b) of rats during NADPH-dependent LPO. 1) Thymectomized rats, 2) thymectomized rat receiving thymosin.

after thymectomy changes took place in the intensity of LPO (spontaneous oxidation was reduced but ascorbate- and NADPH-dependent oxidation was increased) the changes were most marked at later stages of the experiment (on the 190th and 370th days).

Microsomal membranes are a good substrate for nonenzymic Fe^{2+}-ascorbate-dependent, and also enzymic NADPH-dependent LPO [1, 4, 5]. In this connection, we studied the intensity of enzymic LPO simultaneously in liver microsomes and peripheral blood lymphocytes of the thymectomized rats (on the 190th and 370th days). Thus the MDA concentration at these times of the experiment was considerably higher than in the control in both microsomes and lymphocytes.

Consequently, thymectomy causes intensification of phospholipid peroxidation in animals, leading to the accumulation of toxic products (LPCh, conjugated dienes, etc.) and changes in structural components of the biomembranes.

Injection of thymosin into thymectomized animals at different times after the operation led to restoration of the intensity of LPO in all samples, but later it had a positive action, leading to their normalization.

Thus thymus hormones have a marked stabilizing action on the intensity of peroxidation not only in immunocompetent cells, but also in the liver; this is evidently one of the main mechanisms of regulation of the phospholipid composition of biomembranes. Lowering of the spontaneous MDA level in thymectomized animals can evidently be explained by the accumulation of intermediate products of LPO, namely diene conjugates [1]. The reason is evidently that to maintain the necessary

physiological level of a number of biologically active compounds (prostaglandins, thromboxanes, prostacyclines, leukotrienes), which participate in many vitally important metabolic processes, enzymic peroxidation of biomembrane phospholipids takes place under normal conditions in the body Biosynthesis of the above-mentioned substances is known to proceed through a stage of peroxide derivatives of polyunsaturated fatty acids.

An increase in the MDA concentration in the spontaneous LPO system after injection of thymosin is evidently connected with intensification of protein and nucleic acid biosynthesis and also with restoration of the functional activity of the T-components of the immune system under the influence of thymus hormones. All this is evidence that thymus hormones are involved in the regulation of LPO in membranes of immunocompetent cells and in subcellular structures of the liver.

These positive results from the use of thymus hormones thus show that the immunostimulating, biosynthetic, and antioxidative effect of these substances in cytoplasmic structures and in plasma membranes of cells is a very important mechanism of their biological action.

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