USING LIPOSOMES TO CORRECT RESPIRATORY ANOXIA IN EXPERIMENTAL PNEUMONIA

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Most pathological conditions of the lung are accompanied by the development of respiratory anoxia, which leads to disturbances of external respiration, to the appearance of arterial anoxia, and to impairment of the O_2 supply to the tissues [5, 6, 14]. In turn, impairment of the O_2 supply to the tissues causes incompletely oxidized metabolic products to accumulate in the body, the development of metabolic acidosis [4], and activation of lipid peroxidation (LPO) [11]. One of the chief causes of arterial anoxia under these circumstances is reduction of the rate of O_2 diffusion through the air–blood barrier (ABB) of the lungs [13]. Meanwhile the writers have shown that injection of liposomes during acute anoxia increases the rate of O_2 diffusion through the ABB of the lungs and makes oxygenation of the blood more effective in the lungs, thereby having a positive effect on body metabolism [1].

The aim of this investigation was to study the possibility of improving oxygen transport from the air into the blood with the aid of liposomes in animals with experimental pneumonia.

EXPERIMENTAL METHOD

Acute focal pneumonia was produced in laboratory albino rats weighing 100-160 g by the method in [3]. Four days after the development of focal inflammation of the lungs some of the experimental animals inhaled liposomes, by means of a TUR USI-50 ultrasonic inhaler (East Germany), in a dose of 2.5 mg lipid/100 g body weight. The liposomes were prepared from ovolecithin by the method described previously [8]. On the 8th day of development of the diseases the basic parameters of external respiration, the circulation, and gas exchange of the experimental animals were recorded by means of an automated system based on the "Élektronika MS 0401" microcomputer. The partial pressure of oxygen (p_{O_2}) and pH of the arterial blood (carotid artery) were recorded on a "Radelkis" (Hungary) apparatus, and the lactate concentration (C_L) was determined by the method in [12]. The state of LPO was judged by the malonic dialdehyde (MDA) level in the blood, determined by the method in [7].

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the development of acute focal pneumonia led to a marked fall of the tidal volume (V_t), the respiratory minute volume (V_e), and the alveolar ventilation (V_a). Reduction of the O_2 supply to the gas-exchange surface of the lungs, together with reduction of the diffusion capacity of the lungs, arising under these circumstances, led to marked arterial anoxemia, i.e., to the development of respiratory anoxia (Fig. 1). Reduction of the O_2 supply to the tissues led to increased anaerobic glycolysis, accompanied by a 2.1-fold increase in the lactate concentration and by metabolic acidosis (Table 2). The increase observed in the blood MDA concentration (by 2.9 times) is evidence of activation of LPO processes in biological membranes and, together with lactate accumulation, this may lead to destruction of the membranes [2].

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TABLE 1. Basic Parameters of External Respiration and Diffusion Capacity of the Lungs in Rats with Experimental Pneumonia

Parameter	Initial state	Acute pneumonia	
		8th day of development of disease	8th day of development of disease + four inhalations of liposomes
Respiration rate (r), min^{-1}	82,8±7,30	97,40±2,40	82,40±10,30
Tidal volume (V_t), ml/100 g	0,91±0,09	0,41±0,07	0,85±0,05*
Respiratory min. vol. (V_e), ml/min·100 g	47,4±3,5	25,2±2,3	48,4±6,5*
Alveolar ventillation (V_a), ml/min·100 g	73,7±1,3	47,9±4,4	71,3±6,3*
Diffusion capacity of the lungs (DL), mmoles/min·kPa	0,36±0,05	0,08±0,01	0,20±0,02*

Lenged. *Significance of differences ($p < 0.05$) after inhalation of liposomes by animals with pneumonia compared with 8th day of development of disease.

TABLE 2. Changes in pH and Lactate and Malonic Dialdehyde Concentrations in Blood of Rats with Experimental Pneumonia

Parameter	Initial state	Acute pneumonia	
		8th day of development of disease	8th day of development of disease + four inhalations of liposomes
pH of arterial blood	7,40±0,01	7,30±0,02	7,37±0,02*
Lactate concentration (C_L), mmoles/liter	2,8±0,5	5,9±0,8	3,1±0,1*
MDA concentration, μmoles/liter	1,26±0,06	3,72±0,31	2,29±0,63*

Lengend. *Significance of differences ($p < 0.05$) after inhalation of liposomes by animals with pneumonia compared with 8th day of the disease.

Inhalation of liposomes helped to normalize the parameters of external respiration and to increase the diffusion capacity of the lungs (Table 1). As a result the arterial hypoxemia was virtually abolished. Incidentally, the P_{O_2} level in mixed venous blood and in the tissues was not increased quite so much (Fig. 1), evidently due to disturbances of the central and peripheral hemodynamics, i.e., the cardiac output remained low. As a result, despite the increase of P_{O_2} in the arterial blood, the normal O_2 supply to the tissues was not restored. Nevertheless, the lactate concentration and pH of the blood under these conditions came close to their initial level, but the MDA concentration, reflecting LPO processes in the body, fell significantly (Table 2). Normalization of the MDA and lactate concentrations and the pH of the blood after inhalation of liposomes by the experimental animals could be connected with a nonspecific detoxication effect of the phospholipid vesicles, which we observed previously [1, 9].

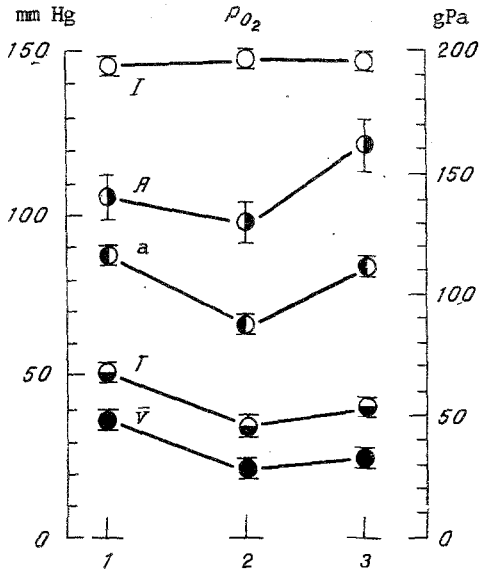

Fig. 1. Partial pressure of O_2 in inspired (I) and alveolar (A) air and in arterial (a) and mixed venous ($\bar{V}$) blood and in tissue capillary blood (T) of rats in initial state (1), on 8th day of development of acute pneumonia (2), and after inhalation of liposomes by animals with pneumonia (3).

After inhalation of liposomes, the macroscopic foci of pneumonia were no longer present, i.e., liposomes have an anti-inflammatory effect. This effect can be explained by activation of the body macrophages, which the writers demonstrated previously in experiments in which phospholipid vesicles were administered to experimental animals with Lewis carcinoma [10].

Inhalation of liposomes by animals with experimental pneumonia thus has a marked anti-anoxic effect, improves metabolic processes, and activates the nonspecific immune system of the experimental animals.

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