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EFFECT OF POST-TRAUMATIC FLUCTUATIONS OF ARTERIAL PARTIAL OXYGEN PRESSURE ON INTENSITY OF LIPID PEROXIDATION IN THE LUNG, LIVER, AND MYOCARDIUM OF RATS WITH LUNG CONTUSION

V. I. Kulitskaya and G. V. Murzin

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A frequent complication of closed chest injury is the development of respiratory insufficiency of arterial hypoxemic type [6, 12], accompanied by metabolic disorders in the tissues [5]. Many mechanisms of these disorders have not yet been studied. In particular, we have no data on the changes in intensity of lipid peroxidation (LPO), activation of which accompanies many pathological states [2, 7, 8, 14] and depends on the partial pressure of oxygen (pO_2) [4, 15].

The main aim of the present investigation was to determine the effect of post-traumatic fluctuations of pO_2 in blood flowing to the tissues, i.e., the partial pressure of oxygen in arterial blood (p_aO_2), on LPO in the lungs, myocardium, and liver in the acute period of closed chest injury.

EXPERIMENTAL METHOD

Experiments were carried out on 155 male Wistar albino rats weighing 250-300 g. Closed chest injury (contusion of the lungs) was produced in animals fixed with the chest uppermost, under ether anesthesia by a shot from a pistol, to the spring of which a plate 20 mm long, 5 mm wide, and 5 mm thick was soldered through a rod. A blow of equal force was applied to the chest at a distance of 1 cm to the right of the sternum (along the sternum).

The value of p_aO_2 was measured in the rats of group 1 on a micro-Astrup apparatus (from Radiometer, Denmark). Arterial blood was taken by puncture from the left ventricle of rats fixed in the prone position before trauma as in the rats of group 1, and LPO was studied after decapitation (5-10 rats at a time) in homogenates of myocardium, liver, and lungs by estimation of the reaction product of decomposition of peroxides, namely malonic dialdehyde (MDA) with thiobarbituric acid [2] per milligram protein, estimated by the method in [2]. The rate of lipid peroxidation was taken to be the ratio between the quantity of MDA formed in the sample after incubation for 2 h at 37°C and the MDA content before incubation. The results were analyzed by computer, using Student's test.

EXPERIMENTAL RESULTS

At autopsy during the first few hours after trauma hemothorax was found in 48% of the rats, and all of them had pleural and subpleural hematomas in the superior and middle lobes of the right lung, which began to absorb

Laboratory of Experimental Pathology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow.
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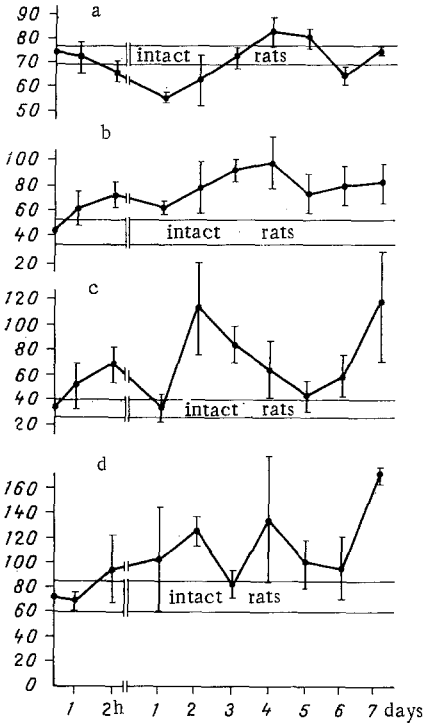

Fig. 1. p_aO_2 (a) and MDA content in homogenates of lungs (b), myocardium (c), and liver (d) in early post-traumatic period of contusion of the lungs (M ± m). Abscissa, time after contusion of the lungs; ordinate: a) mm Hg; b, c, d) nanomoles/mg protein.

after 3 days. By the end of the first week either absorbing hematomas or traces of absorbed hematomas were observed in the superior and middle lobes of the right lung of the majority of rats. In none of the rats examined were any mechanical injuries found in the myocardium and liver, and also in the left lung.

The mean value of p_aO_2 in the intact rats was 73 ± 3.45 mm Hg. The concentration and rate of accumulation of MDA were minimal in lung tissue homogenates, and maximal in the liver. The myocardium occupied an intermediate position as regards this parameter (Fig. 1).

During the first few hours after injury to the lungs the rats showed a tendency to develop arterial hypoxemia, and at the same time, MDA accumulated in homogenates of the myocardium, lungs, and liver to higher levels than in the corresponding tissues of intact rats, but the difference was statistically significant only in myocardial homogenates (Fig. 1).

Later arterial hypoxemia was observed 1 and 6 days after trauma, whereas recovery of p_aO_2 took place 2-5 and 7 days after trauma (Fig. 1a). Accumulation of MDA in homogenates of the myocardium, lungs, and liver was observed, not in the period when marked arterial hypoxemia was recorded, but in the period of recovery of p_aO_2: in the injured lung tissue simultaneously with recovery of p_aO_2 (2-4 and 7 days after trauma), but in the myocardium and liver, in each case on the day after arterial hypoxemia was recorded (2 and 7 days after trauma). The rise of p_aO_2 to its level in intact rats was combined with a gradual decrease in the MDA concentration in myocardial homogenates up to the level of MDA in the myocardium of intact rats, and with partial normalization of its concentration in liver homogenates (Fig. 1a-d).

The rate of lipid peroxidation in homogenates of the myocardium, lungs, and liver began to fall in the first few hours after trauma and remained low until the end of the observations, except for the period of recovery of p_aO_2 3-5 days after trauma, when it rose in all tissues to the same level as the rate of lipid peroxidation of the corresponding tissues of intact rats, and in homogenates of lung tissue it actually rose above that level (Fig. 2).

Activation of LPO in homogenates of the myocardium, lungs, and liver thus showed definite correlation with changes in p_aO_2 during the first week after lung damage. However, in the first few hours after trauma (shock period) activation of LPO in all tissues and, above all, in the myocardium was evidently determined not

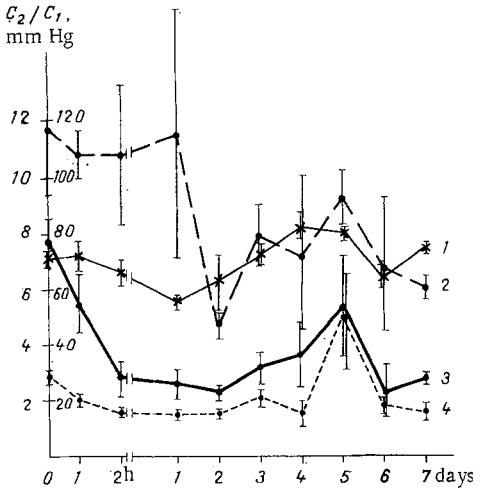

Fig. 2. p_aO_2 (1) and rate of lipid peroxidation in homogenates of liver (2), myocardium (3), and lungs (4) in the early post-traumatic period of contusion of the lungs (M ± m). Abscissa, time after contusion of the lungs; ordinate, ratio of MDA concentration in tissue homogenates after incubation for 2 h at 37°C to MDA concentration in homogenates before incubation (C_2/C_1) and p_aO_2 (in mm Hg).

only by the appearance of respiratory insufficiency, but also by the response of the animal to trauma as a whole: to pain stress, to blood loss, and so on [2, 7]. Absence of activation of LPO in the presence of marked arterial hypoxemia in the first days after trauma can, however, be explained by the high concentration of antioxidants in the tissues and by their possible redistribution between the tissues in the acute period of trauma [2, 3]. A sharp increase in the intensity of LPO in homogenates of myocardium and liver in the initial stage of restoration of p_aO_2, i.e., the appearance of a state of "relative hyperoxia" [1], or the oxygen paradox [8], in the tissues is in agreement with data in the literature and is explained by exhaustion of reserves of antioxidants appearing in the tissues during the period of hypoxia [1, 2, 4].

Activation of LPO in lung tissue, arising simultaneously with restoration of p_aO_2, may indicate an increase in sensitivity of the injured lung tissue to the toxic action of O_2 [11, 14] and it evidently arises through the increased inflow of O_2 to the pulmonary alveoli in the period of restoration of p_aO_2 [10]. The increase in sensitivity of the injured lung tissue to the toxic influence of O_2 is found in the period of trauma when the arrival of blood with a high pO_2 is essential for restoration of metabolism of the liver and, more especially of the myocardium. It can also be postulated that because of the inequality of lung ventilation, which is observed in this period of trauma [6], the formation of additional oxygen radicals and peroxides takes place in ventilated and hyperventilated areas of the lungs.

Intensification of LPO in the lung tissue may be a risk also for other tissues, since lipid peroxides may be carried from the lungs with the blood stream into the systemic circulation, for example, into the myocardium, as is shown by the high direct correlation found between the MDA concentration in homogenates of the myocardium and lungs ($R = 0.81$, $P < 0.01$).

Accumulation of LPO products in the myocardium, lungs, and liver in the early post-traumatic period could be inhibited somewhat because of a decrease in the rate of lipid peroxidation. However, since the degree of manifestation of this protective reaction depends not only on a possible change in composition of the tissue lipids [9, 13], i.e., on accumulation of less oxidizable lipids in them, but also on the quantity of O_2 reaching the tissues [2, 4], it could be seen to be weakened a little in the period of restoration of p_aO_2, especially in damaged lung tissue.

The results thus show that restoration of the pulmonary gas exchange in the early post-traumatic period has a favorable influence on oxidation-reduction processes in the myocardium, improves them somewhat in the liver, but at the same time, even when room air is breathed, it leads to some increase in the intensity of free oxidation in the injured lung tissue. This suggests that oxygen therapy, undertaken on casualties in this category

in the early period after trauma may be useful for restoring metabolism in the myocardium and liver, if not injured during trauma, but may nevertheless induce additional disturbances in the lung tissue itself.

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ACTIVATION OF THE BLOOD KALLIKREIN – KININ SYSTEM DURING DISSEMINATED INTRAVASCULAR CLOTTING IN RATS. ROLE OF THE PULMONARY COMPONENT AND ATTEMPTED CORRECTION WITH ASPIRIN

G. N. Meshcheryakov and O. A. Gomazkov

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Disseminated intravascular clotting (DIC) and associated disturbances of the rheologic properties of the blood and of the microcirculation are widespread complications of severe trauma [7]. Disturbances of regulation of the clotting and fibrinolytic systems of the blood with multiple microthrombus formation arising in this form of pathology lead to disturbance of functions of the brain, kidneys, lungs, and other systems of the body and may frequently cause the formation of "shock organs." In the multicomponent mechanism of the initial phase of the pathogenesis of DIC disturbances of regulation of the liquid state of the blood must be distinguished: marked activation of the clotting system, a fall in platelet concentration, massive formation of degradation products of fibrinogen, release of vasoactive substances into the blood stream leading to changes in capillary permeability and the microcirculation [1, 8]. To formulate the purpose of the investigation three interconnected lines can be distinguished: 1) The kallikrein–kinin system (KKS) is one of the most important systems in regula-

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Research Laboratory of General Resuscitation, Academy of Medical Sciences of the USSR. Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow.

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