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EFFECT OF LIPID PEROXIDATION IN THE LUNGS ON ARTERIAL HYPOXEMIA DEVELOPMENT IN RATS SOON AFTER TRAUMA

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UDC 616.24-001-07:616.24-008.939.
15-39-06:616.152.21-008.64

KEY WORDS: respiratory insufficiency; lipid peroxidation

After injury to the lungs the residual portions undergo hyperventilation [9], and this induces the accumulation of lipid peroxides and free radicals in them [11, 13, 15]. However, the relative importance of activation of lipid peroxidation (LPO) in the lungs, which requires O_2 for it to proceed [1], in the development of post-traumatic arterial hypoxemia, which often appears in the period immediately after closed chest trauma and is responsible for its unfavorable course [7], is not yet clear. The aim of this investigation was to determine the role of these processes in the mechanism of the fall of p_aO_2 in the early post-traumatic period following contusion of the chest in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 135 male Wistar rats weighing 200-250 g. Contusion of the lungs was produced by means of a spring-operated pistol. A blow of measured force was applied to the right half of the chest as described previously [5]. As a result of trauma the upper and cardiac lobes of the light lung (RL) were injured, whereas in the left lung (LL) no mechanical injury was produced. To analyze the time course of their state rats were decapitated before trauma (intact rats), 1 and 2 h after trauma, and every subsequent day until the 7th day inclusive, with 10-12 animals used at each time. Before sacrifice, the rats were bound in the prone position and their respiration rate (RR) and fO_2 value, i.e., the difference between the O_2 concentration in the inspired air (21%) and the O_2 concentration in the end-expired air, measured with a MKh-6202 gas analyzer. The parameter fO_2 was used to char-

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 0007-4888/87/0008-1060 $12.50

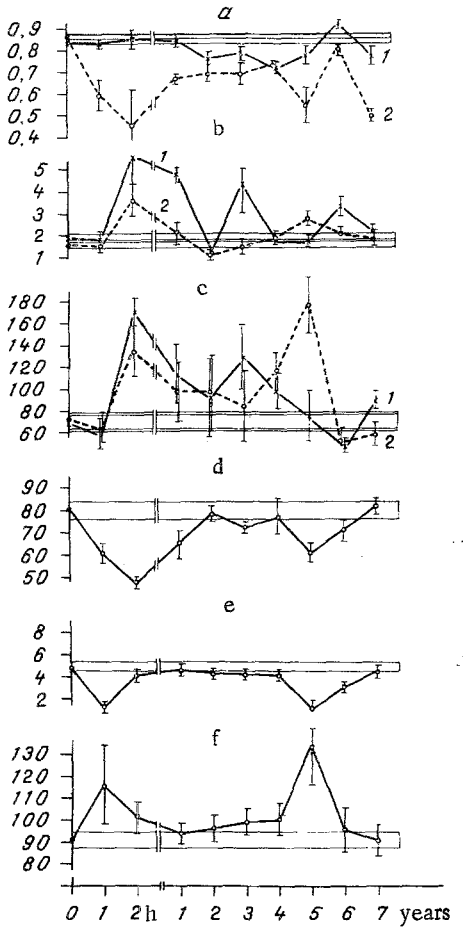

Fig. 1. Surfactant activity (a), intensity of ChL (b), and MDA concentration (c) in LL (1) and RL (2), and values of p_aO_2 (d), fO_2 (e), and RR (f) in rats in the early post-traumatic period (contusion of the chest). Abscissa, time after contusion of the lungs; ordinate: a) relative units; b) signal to background ratio (in relative units); c) nmoles/mg protein; d) mm Hg; e) %; f) number of respiratory cycles per minute. Continuous horizontal lines show region of change of parameter in intact animals.

acterize changes in the relative depth of respiration. Arterial blood was obtained from the left ventricle of the rats by puncture for determination of p_aO_2 on a Corning gas analyzer (England).

Surfactant activity, the malonic dialdehyde (DMA) concentration, and the intensity of chemiluminescence (ChL) of total lipids were measured separately in the injured RL and intact LL. Surfactant activity (average) in the lung was measured by the method in [14]. The MDA concentration was determined with the aid of 2-thiobartituric acid [4] in nanomoles/mg protein (Kjeldahl's method [18]). Total lipids were isolated by the method in [12]. ChL was recorded by a chemiluminescence system with the FE-85 "Radiometer 20 046" instrument (East Germany).

EXPERIMENTAL RESULTS

During the first hour after trauma to the rats' chest p_aO_2 fell sharply from its initial level ($p < 0.05$). This took place against the background of an increase in RR and a decrease in fO_2, while the MDA level and intensity of ChL of total lipids in RL and LL remained unchanged: surfactant activity fell in RL ($p < 0.01$) and remained unchanged in LL.

Arterial hypoxemia continued to increase 2 h after trauma, although the character of ventilation at this period returned to its initial form. The fall of p_aO_2 was accompanied by a sharp increase in the MDA concentration and intensity of ChL in both lungs (it was more marked in LL than in RL (Fig. 1)). These changes developed against the background of a progressive decrease in surfactant activity in RL and a small increase in LL.

A tendency for the value of p_aO_2 to be restored appeared 24 h after trauma, and after 48 h it no longer differed from its value in intact rats. At this period the character of the total pulmonary ventilation (RR and fO_2) did not differ significantly from its initial form. A tendency appeared toward normalization of the MDA concentration and intensity of ChL in both lungs, and also of surfactant activity in RL; however, this parameter still remained lower than initially ($p < 0.01$). As before, surfactant activity in LL remained at its initial level.

During further observations until the end of the first week after trauma fluctuations in the pulmonary gas exchange were noted. Arterial normoxemia was recorded on the 4th and 7th days after trauma, against the background of initial values of pulmonary ventilation, MDA concentration, and intensity of ChL in both lungs, although surfactant activity was reduced in both RL and LL. A tendency toward the appearance of arterial hypoxemia was found on the 3rd and 6th days, when ventilation was normal. On the 3rd day accumulation of MDA and an increase in the intensity of ChL were observed in LL, while on the 6th day the intensity of ChL was still increased in LL. Marked arterial hypoxemia occurred on the 5th day after chest trauma, against the background of a disturbance of total pulmonary ventilation and MDA accumulation, and of activation of ChL in RL. Surfactant activity was reduced in both lungs from the 3rd until the 7th days, except on the 6th day, when in both lungs it regained its initial value.

Surfactant activity in the injured RL in the early post-traumatic period was inversely proportional to the MDA concentration and the intensity of ChL, whereas in the intact LL, on the contrary, it was directly proportional. The coefficient of correlation between surfactant activity and ChL in LL was 0.67 ($p < 0.01$).

The results suggest that oxygen-dependent processes, whose intermediate products are peroxides and free radicals, participate in the development of arterial hypoxemia: every fall in the value of p_aO_2 in the early period after contusion of the chest, except the first hour after tramua, was accompanied by activation of LPO in both lungs or in one lung. However, the relative importance of activation of these processes in the lungs and the fall in the value of p_aO_2 cannot be determined because disturbances at the submolecular level appeared in the lungs simultaneously with changes of function: quickening of respiration and a decrease in its depth, indicating an increase in ventilation of the dead space [9] and a decrease in surfactant activity in both lungs or in one lung, evidence of reduction of the ventilating surface of the lungs and damage to the alveolar-capillary membrane [3].

However, LPO in the lungs can evidently exert its own influence on gas exchange in the lungs, first, because it is accompanied by utilization of O_2 [1] and, second, it damages cell membranes [4], which reduces their permeability for O_2 [2]. These processes can reduce the quantity of O_2 reaching the erythrocytes in the pulmonary capillaries and can aggravate the degree of arterial hypoxemia.

Even though activation of LPO in RL and LL during the first hours and days after trauma appeared simultaneously, the sources of the lipid peroxides appearing in the damaged and intact regions of the lungs were evidently different oxygen-dependent processes. Intensification of LPO in RL, arising simultaneously with a decrease in surfactant activity, i.e., with inhibition of surfactant synthesis [3], points to activation predominantly of catabolic reactions in the injured regions and, in particular, of processes of phagocytosis, including the generation of active forms of O_2 [6]. Intensification of LPO in LL, arising simultaneously with the increase in surfactant activity, i.e., with intensification of surfactant synthesis, indicates activation mainly of anabolic reactions in the intact regions and, in particular, intensification of synthesis of phospholipids (substrates of LPO). All the processes mentioned above utilize O_2, which, in the lungs, they evidently obtain from the alveoli. Activation of LPO in the lungs during the first hours and days therefore depended not only on reserves of antioxidants [10], but also on the character of pulmonary ventilation, determining the supply of O_2 to the alveoli [9], whereas later it also depended on the accumulation of saturated fatty acids in the hyperventilated regions of the lungs [14].

Activation of LPO in the lungs in the early post-taumatic period may therefore be one cause of the worsening of the degree of respiratory insufficiency of arterial-hypoxemic type. It is perhaps one of the processes which cause increased O_2 consumption in the lungs in the acute period of closed chest trauma.

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EFFECT OF DIETARY LINOLEIC ACID CONTENT OF PLATELET AGGREGATION AND CALCIUM SENSITIVITY AND ON MICROVISCOSITY OF PLATELET MEMBRANES IN RATS

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UDC 612.111.7-06:613.288:547.396

KEY WORDS: linoleic acid; aggregation; platelets; diet

Diets rich in saturated or polysaturated fatty acids (PUFA) have opposite actions on platelet (PL) function in man [5, 8-10] and experimental animals [12, 13, 15]. It is claimed that the action of such diets is based on food modification of the PL spectrum of PUFA, which are precursors of the eicosanoids in phospholipid membranes, and this leads to changes in the synthesis of compounds (such as thromboxane A_2, prostaglandins E_1 and E_2, etc.) which have a powerful effect on the development of PL aggregation [12]. Meanwhile reception of the inducer of PL aggregation and their response to it depend on the state of the membrane, in which lipids are one of the principal structural components. However, the concrete mechanisms of the effect of food fatty acids on PL have not been finally established. There are contradictory data, due to differences in the duration of exposure, the species of the experimental animals [15], the quantity and quality of PUFA in the diet, and so on.

The aim of this investigation was to study the characteristics of aggregation of PL and their sensitivity to Ca^{++} and the microviscosity of PL membranes in rats receiving diets differing in their linoleic acid (LA) content.

EXPERIMENTAL METHOD

Three semisynthetic diets, equal in calorific value but differing in their LA (18:2n6) content: diet I) 0.1 calorie % (cal. %) of LA; II) 9.0 cal. % of LA; diet III) 16 cal. % of LA. The diets were made up by V. V. Atrokhov, on the staff of the authors' laboratory, on a basis of data in the literature [1] and they included a fat-free basis together with a mixture of water-soluble vitamins in casein with the addition of fatty components: for diet I) 11% of hydrogenated sunflower oil (Salomas) and 1% of a mixture of fat-soluble vitamins in Salomas; for diet II) 4% of sunflower oil, 5% of lard, 2% of Salomas, and 1% of a mixture of fat-soluble vitamins in sunflower oil; for diet III) 10% of sunflower oil, 1% of lard, and 1% of a mixture of fat-soluble vitamins in sunflower oil. The mineral composition of the diet was supplied by the addition of Jones—Foster salt mixture [1] supplemented by fluorine (0.86 mg/100 g of dry food mixture). To prepare the diets all the ingredients were finely ground, and mixed uniformly to obtain a homogeneous powdery mass, which was kept at −20°C. If necessary

Laboratory of Pathophysiology, Research Institute of Pediatrics, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR M. Ya. Studenikin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 104, No. 8, pp. 160-162, August, 1987. Original article submitted October 2, 1986.

0007-4888/87/0008-1063 $12.50