PULMONARY CIRCULATION IN EXPERIMENTAL TOXIC EDEMA OF THE LUNGS

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KEY WORDS: pulmonary circulation; experimental edema of the lungs; cardiac ejection; ultrasound; pulsatile blood flow.

The development of edema of the lungs is based on two principal mechanisms: a rise of capillary hydrostatic pressure and an increase in vascular permeability for proteins. These factors create conditions which disturb the water balance in the lungs, when transvascular filtration of the liquid part of the blood begins to exceed the rate of absorption and the rate of drainage of lymph from the lung tissue [1, 2, 10, 12, 15]. A major role in the formation of these conditions is played by the pulmonary circulation. Data on changes in the individual parameters of the hemodynamics of the pulmonary circulation (pressure in the pulmonary artery, resistivity of the pulmonary vessels, cardiac output, etc.) have been obtained mainly in the late stages after injury to the lung vessels by various agents used to simulate pulmonary edema, namely after 60-120 min or more, against the background of established edema (9-11]. Meanwhile, it is important to know the time course of changes in the pulmonary circulation arising immediately after the action of a toxic agent on the vascular bed of the lungs, and which are accompanied by the development of edema. Comparison of the character and order of the changes in the set of parameters for the pulmonary circulation may be helpful in the analysis of mechanisms determining the development of pulmonary edema.

The aim of this investigation was to study the blood flow in different parts of the vascular bed of the lungs and the blood pressure in the pulmonary artery, and also to compare the minute ejection volume of the right and left sides of the heart during the development of acute experimental edema of the lungs.

EXPERIMENTAL METHOD

The blood flow in the artery and vein of the lower lobe was studied by an ultrasonic method [3] in acute experiments on 35 male cats weighing 3-5 kg with an open chest and artificial ventilation of the lungs, and under pentobarbital anesthesia (30-40 mg/kg, intraperitoneally). The method used to study the pulmonary circulation was described previously [7]. The blood pressure in the pulmonary artery was recorded by means of an electromanometer [4]. The catheter was introduced through the upper lobar pulmonary artery into the lumen of the left pulmonary artery. The resistance of the vascular bed of the lungs was recorded by means of an analog computer system (of our own design) as the quotient obtained by dividing the mean values of pressure by the mean value of the blood flow in the pulmonary artery, in mm Hg/(ml/min). The pressure was measured in the femoral artery and, in some experiments, in the left atrium. In experiments on 12 animals a parallel study was made of the blood flow in the ascending aorta and the infundibulum. The balance between ejection from the right and left ventricles was evaluated by means of an analog computer as the ratio of the mean values of the blood flow through the infundibulum and the ascending aorta. Six experiments were carried out with a closed chest and with natural breathing. Acute edema of the lungs was simulated by intravenous injection of a mixture of fatty acids and olive oil (composition of the mixture: caproic acid 3.8 g, caprylic acid 3.1 g, olive oil 3 g) in a dose of 0.02-0.04 ml/kg [14]. All the parameters were recorded for 60-120 min after injection. The fatty acids have a direct toxic action on the capillary bed of the lungs, disturbing permeability of the vascular wall, which leads to increased transport of water and protein into the interstices, followed by the development of pulmonary edema [10]. The degree of edema was assessed as the

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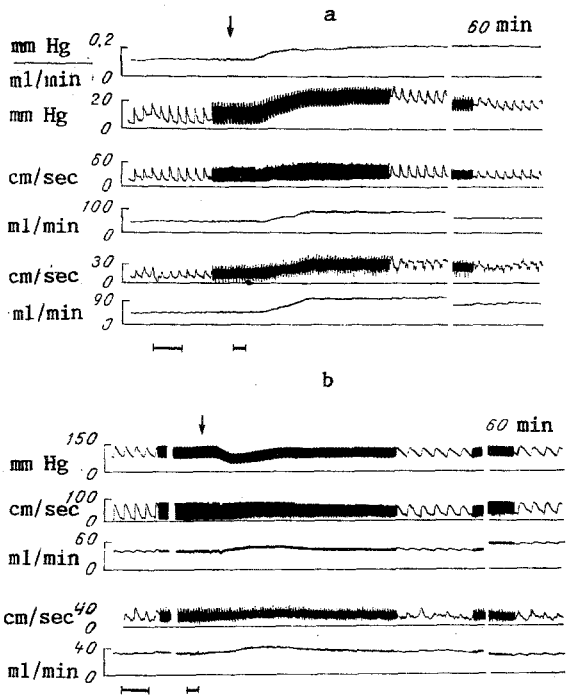

Fig. 1. Changes in parameters of pulmonary and systemic hemodynamics in response to injection of fatty acids. From top to bottom: a) resistivity of vascular bed of the lungs, blood pressure in pulmonary artery, phasic blood flow in artery of lower lobe, average values of flow in artery of lower lobe, phasic blood flow in vein of lower lobe, average values of flow in vein of lower lobe; b) pressure in femoral artery, phasic blood flow in artery of lower lobe, average blood flow in artery of lower lobe, phasic blood flow in vein of lower lobe, average values of flow in vein of lower lobe. Here and in Figs. 2 and 3: thin straight lines beneath each curve indicate zero levels. Arrow indicates time of injection of mixture of fatty acids into femoral vein. Time scale: 1 and 10 sec; 60 min denotes 60 min after injection of fatty acids.

pulmonary coefficient (normally 5.5-6 in cats) and on the basis of dry residue (normally 18-20%) [2]. At the end of the experiments the pulmonary coefficient averaged 10.5 (from 7.4 to 17.8); the average value based on dry residue was 13.3% (varying from 11 to 15.4%).

EXPERIMENTAL RESULTS

After injection of the fatty acids in pressure in the pulmonary artery increased considerably (by 2-2.5 times). The volume velocity of the blood flow along the artery of the lower-lobe artery and vein increased by 17-50%, on average by 38% (Fig. 1). Changes in the blood flow and pressure in the pulmonary artery began simultaneously, 10-20 sec after injection of the preparation. The blood flow reached a maximum after 1-2 min, after which the time course of its changes varied. In most experiments the blood flow in the artery and vein remained increased for 30-60 min and then began to fall gradually down to or below the initial value (Figs. 1a and 2a). In other experiments, the increase in blood flow was of relatively short duration: the original value was restored after 3-5 min. In individual experiments the inflow of blood into the artery continued to increase with the passage of time, whereas the outflow along the vein gradually decreased (Fig. 1b).

The blood pressure in the femoral artery reached a maximum 3-5 min after injection of the preparation and usually remained at that level for 30-60 min or more. The resistance of the vascular bed of the lungs during the first minutes increased parallel to the pressure in the pulmonary circulation; later in the course of the experiment it gradually fell, but still remained higher than initially (Fig. 1a). The average pressure in the left atrium was unchanged. It can be concluded from these results that under these conditions the capillary hydrostatic pressure in the lungs rose.

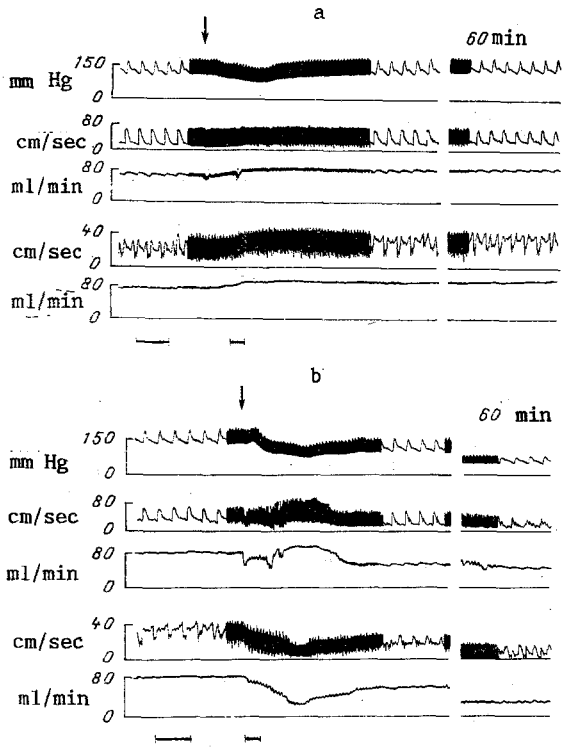

Fig. 2. Changes in pulmonary circulation in response to first (a) and repeated (b) injections of fatty acids. Legend as to Fig. 1b.

The systemic arterial pressure fell after injection of the preparation by 20-50 mm Hg (see Figs. 1b, 2a, and 3a, b). The beginning of the fall in the systemic arterial pressure coincided in time with the beginning of response of the parameters of the pulmonary circulation (Figs. 1a and 2a). Baroreceptors, embodied in the vascular walls, afferent signals from which travel along the vagus nerve to the vasomotor center, where efferent signals to the heart and systemic vessels are formed, and as a result of which the systemic vessels dilate, are activated in response to a rise of pressure in the vascular system of the lungs [1, 5]. Under physiological conditions this response leads to reduction of the inflow of blood into the right heart and unloading of the pulmonary circulation when the pressure in it rises [1]. However, under pathological conditions this does not happen, as will be shown below. The systemic arterial pressure reaches a minimum in the course of 1-1.5 min, after which it reverts to its initial value (or not quite to it), despite the fact that the pressure in the pulmonary system remains raised.

In response to injection of the fatty acids the character of the phasic blood flow in the artery and vein of the lower lobe changed. An increase in the volume velocity of the blood flow in the pulmonary artery and vein took place on account of an increase in the constant component (the diastolic inflow), as can be seen in Figs. 1a, b, and 2a. Previously we observed this same fact when studying the effect of anoxia and hypercapnia on the pulmonary circulation [8]. In the present study a considerable change was discovered also in the shape of the curve of phasic blood flow in the artery: parallel with an increase in the diastolic flow, the steepness of rise of the systolic component of the total flow decreased and the curve became rounded in shape (Figs. 1 and 2a). From a consideration of all these changes in the shape of the pulsatile blood flow, we can postulate a reduction of tone of the pulmonary arteries [8], a decrease in rigidity of the vessel wall [6], probably due to injury by injection of the preparation.

Accordingly, the increase in blood pressure in the system of the pulmonary artery and the sharp increase in its resistance are not fully understood. It can be tentatively suggested that the toxic action of fatty acids on the vascular bed of the lungs is accompanied by additional rheologic disorders, and intravascular aggregation of blood cells, thus creating an additional resistance to the blood flow due to accompanying microembolism [10]. The effect of the arterial hypoxemia developing under these conditions likewise cannot be disregarded [11, 14].

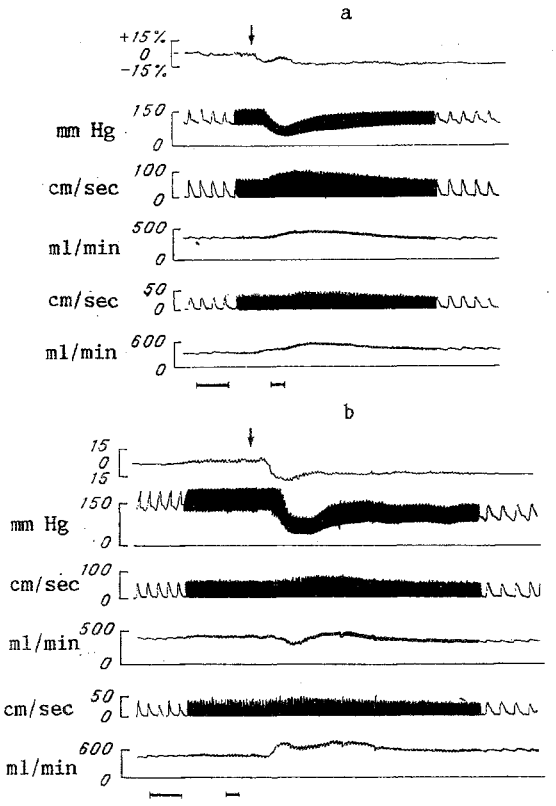

Fig. 3. Changes in blood flow in ascending aorta and infundibulum in response to injection of fatty acids. From top to bottom: balance between ejection volume of right and left ventricles (in relative units) — downward direction of curve corresponds to increase in blood flow in infundibulum relative to blood flow in aorta, arterial pressure in femoral artery, phasic blood flow in ascending aorta, average values of flow in ascending aorta, phasic blood flow in infundibulum, average values of flow in pulmonary artery. Explanation in text.

It is stated in the literature that contractions of the pulmonary veins may have a role in the development of pulmonary edema [12, 13]. Our own data on an increase in volume velocity of the blood flow in the pulmonary vein and an increase in the constant component of the blood flow in response to injection of fatty acids (Figs. 1 and 2a) do not confirm this suggestion, at least for the model of pulmonary edema which we used. However, changes of this kind in the blood flow along the pulmonary veins take place when the fatty acids exerted their toxic action on the intact vascular bed of the lungs. Repeated injection of fatty acids when edema had already developed (40-60 min after the first injection) can induce a sharp decrease in the outflow of blood along the pulmonary veins (Fig. 2b), suggesting that they contract under these conditions. It must be noted that when edema has developed in the lungs, anoxia, hypercapnia, and pharmacological agents also have a similar effect.

The increase in volume velocity of the blood flow in the pulmonary vessels can take place either as the result of a synchronous increase in cardiac ejection volumes of the right and left sides of the heart or as a result of redistribution of blood into the pulmonary circulation. To test these hypotheses, a series of experiments was carried out in which ejection volumes from the right and left ventricles were studied in addition. In most experiments, in response to injection of fatty acids, there was an increase in the volume velocity of the blood flow both in the ascending aorta and in the infundibulum; however, this increase in blood flow in the infundibulum was greater than in the aorta (Fig. 3a). In individual experiments, changes in blood flow were in opposite directions: it fell in the aorta but rose in the infundibulum (Fig. 3b). Redistribution of the blood flow into the pulmonary circulation in half of the experiments began immediately after injection of the fatty acids, but in the remaining experiments it began 3-5 min after their injection.

The results indicate that toxic action on the vascular bed of the lungs causes redistribution of the blood flow into the pulmonary circulation. In a situation when the pulmonary vascular permeability is already disturbed, changes in the balance normally existing between the ejection volumes of the right and left ventricles may aggravate the degree of pulmonary edema.

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REGULATION OF RESPIRATION AND THE CIRCULATION IN MICROEMBOLISM OF PULMONARY VESSELS

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KEY WORDS: microembolism; respiratory center; hemodynamics of the pulmonary and systemic circulations; microcirculation of the lungs.

Microembolism has been discussed mainly by clinicians, who have studied this phenomenon at various levels — from clinical observations to bioclinical investigations [2, 4, 6]. Pulmonary embolism in clinical practice is manifested in several different forms, depending on the rate and intensity of its development. It has been shown that in response to microembolism of the pulmonary vessels, both the pulmonary and the systemic branches of the circulation are involved [9, 11-13]; in microembolism of the pulmonary vessels a threatening complication, namely pulmonary edema, develops.

The aim of this investigation was to compare the time course of the functional state of the respiratory center with the features of pulmonary macro- and microcirculation during microembolism of the pulmonary vessels, with the subsequent development of edema of the lungs.

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