EFFECT OF VARIOUS ARTIFICIAL VENTILATION PROGRAMS ON THE COURSE OF EXPERIMENTAL TOXIC EDEMA OF THE LUNGS

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To correct respiratory failure associated with the development of edema of the lungs (EL) artificial ventilation (AV) is often used under clinical conditions, and the problem of its optimal programs has accordingly been discussed [2, 5]. It has been shown [3] that the use of controlled respiration with increased frequency in man and experimental animals with acute EL reduces the quantity of edema fluid and the degree of hypoxia. According to other workers [2, 7, 9] increasing the rate of ventilation or inflation of the lungs leads to an increase in permeability of the alveolar epithelium, increased filtration from the pulmonary microvessels, disturbance of the lymph drainage, changes in surfactant activity, and consequent increased accumulation of fluid and impaired gas exchange in the lungs. The question of the action of enhanced AV programs on the development of EL remains unsolved. Data likewise are not available on the comparative effect of increasing the frequency or volume of AV on the course of toxic EL.

The aim of this investigation was to study the effect of an increase in frequency or volume of AV on the degree of EL over a period of time, the intensity of foam formation, the pulmonary gas exchange, and the survival rate of the animals after the development of experimental toxic EL.

EXPERIMENTAL METHOD

Experiments were carried out on 60 male cats weighing 2.5-4 kg, anesthetized by intraperitoneal injection of pentobarbital (30-40 mg/kg), under closed chest conditions. Before the beginning of ventilation the animal was immobilized by intravenous injection of turbocurarine (initial dose 2.5 mg/kg, followed by 0.25 mg/kg on the appearance of signs of recovery of respiration). AV was carried out with the aid of a "Vita-1" volume-frequency respirator. The development of EL was investigated, starting from initial parameters of AV that corresponded to natural breathing of the animal in volume and frequency, and to an increased (threefold) frequency or (twofold) volume. Ventilation began 2-3 min before the edema-inducing procedure. A model of LE was created by intravenous injection of a mixture of fatty acids with olive oil in a dose of 0.04 ml/kg [11]. The development of edema was observed for 90 min, for in the course of this time the experimental animals died or the parameters of the degree of EL, gas exchange, and BP stabilized, and remained constant for the next 2-3 h. The degree of EL was estimated by determining the pulmonary coefficient [4] and also the quantity of edema fluid and the additional blood volume in the lungs, calculated by the method in [10]. The survival rate of the animals on different AV programs and the time of appearance of foam in the lumen of the trachea were recorded. The blood pressure (BP) in the femoral artery was measured with an electromanometer. The blood gas composition (pO_2 and pCO_2) was determined by the micromethod of Astrup and Siggaard-Andersen.

The results were analyzed by Student's t test.

EXPERIMENTAL RESULTS

The experiments showed that after receiving injections of fatty acids the experimental animals gradually developed a marked degree of EL. On the initial AV programs the coronary coefficient increased to its highest level during the first 10-15 min after the edema-induc-

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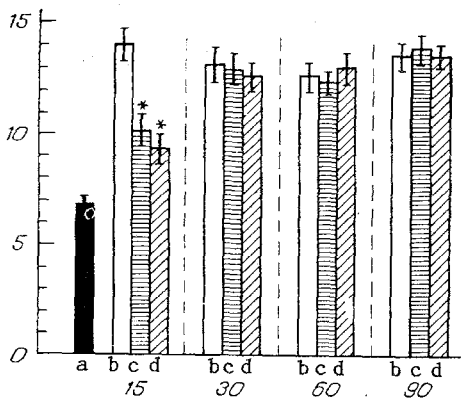

Fig. 1

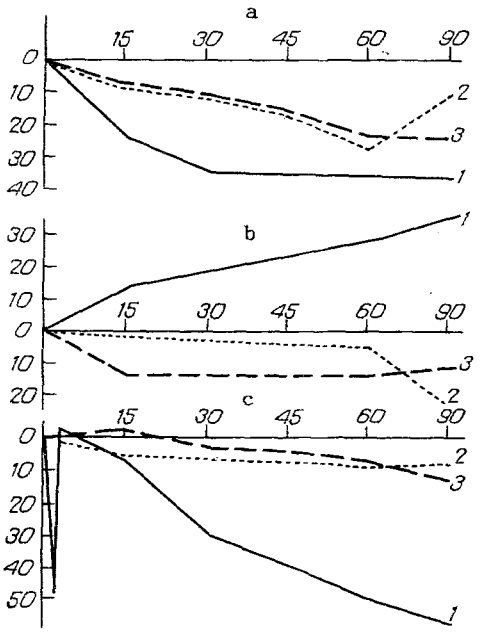

Fig. 2

Fig. 1. Changes in pulmonary coefficient during development of toxic EL against the background of AV under different conditions. Abscissa, time of observation (in min). Here and in Fig. 2: ordinate, pulmonary coefficient (in g/kg); a) pulmonary coefficient before injection of fatty acids; b) with initial AV programs; c) with increase in frequency of AV; d) with increase in volume of AV. Asterisk indicates significant differences in parameter with an increase in frequency and volume of AV compared with initial conditions.

Fig. 2. Time course (in %) of pO_2 (a), pCO_2 (b), and BP (c) during development of EL and with different AV programs. 1) Initial programs; 2) increase of frequency; 3) increase of volume of AV.

ing procedure (Fig. 1). The development of EL against the background of AV with increased frequency of volume led to the greatest increase in pulmonary coefficient by the 30th minute. Changes in the value of the pulmonary coefficient in the first 10-30 min after injection of the fatty acids took place as a result of increased filtration of fluid through the pulmonary microvessels, as shown by an increase in the quantity of edema fluid to 5.5 ± 0.9 g/kg. The added blood volume in the lungs under these circumstances did not exceed 1.0 ± 0.3 g/kg. There is evidence [1, 8] to show that a rise of alveolar pressure in animals with a closed chest leads to a decrease in area of the filtration surface of the pulmonary microvessels or to increased reabsorption in them. In the present investigation, with an increase in the volume of AV of the lungs the tracheal and also, consequently, the alveolar pressure increased at inspiration to 25-30 cm water, but with an increase in the frequency of AV, it rose to 15-20 cm water. It can accordingly be postulated that an increase in the frequency or volume of AV retards the development of EL during the first 20-30 min as a result of reduction of the filtration surface or stimulation of reabsorption. Later, from the 30th to the 90th minute of the investigation, a small change in the value of the pulmonary coefficient took place on account of an increase in the quantity of edema fluid, and it was independent of the conditions of AV.

Thus, the development of toxic EL against the background of an increase in both frequency and volume of AV reduced its degree equally in the initial stages after the edema-inducing procedure and did not affect EL if it had already developed.

Analysis of the blood gas composition showed maximal development of arterial hypoxemia on average by the 30th minute after injection of fatty acids during the initial AV program (pO_2 fell from 94.6 ± 1.9 to 64.12 ± 3.1 mm Hg; Fig. 2a). The greatest fall in pO_2 of the blood occurred on average 60 min after the edema-inducing procedure, when it amounted to 71.3 ± 2.9 mm Hg with an increase in volume and 63.5 ± 3.0 mm Hg with an increase in frequency of AV. In the experiments with an increase in volume of AV the blood oxygen concentration thereafter remained unchanged, but an increase in the frequency of AV led to an in-

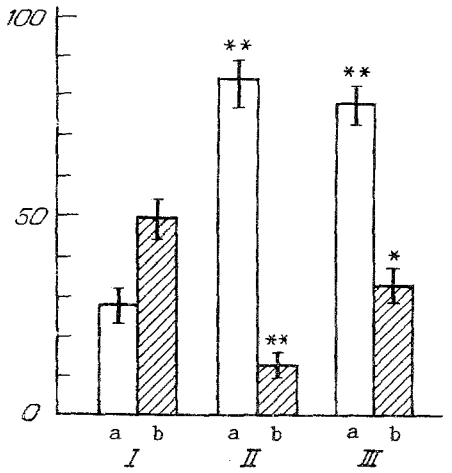

Fig. 3. Survival rate of animals and foam formation during development of EL and with different AV programs. Ordinate: a) number of animals (in %) surviving 90 min after edema-inducing procedure; b) number of cases (in %) of appearance of foam from trachea. I) Original program; II) increase in frequency; III) increase in volume of AV. *$p < 0.05$; **$p < 0.001$ compared with I.

crease in pO_2, which did not differ significantly from the original value (82.3 ± 2.8 mm Hg) by the 90th minute of development of EL. Hence it follows that arterial hypoxemia in response to an increase in the frequency and volume of AV developed much later with the maximal increase in the pulmonary coefficient than with the initial level of ventilation. In the late stages of EL an increase in the frequency of AV facilitated oxygenation of the arterial blood better than an increase in the volume of AV. When EL developed against the background of the initial AV programs pCO_2 of the arterial blood increased by 35% by the 90th minute (Fig. 2b). The increase in the frequency of AV did not lead to any significant changes in pCO_2, but merely caused a decrease of 22% in this parameter after the 60th minute of EL. The course of EL following an increase in the volume of AV was characterized by a fall of pCO_2 by 10-15% during the first few minutes after injection of the fatty acids, and this remained unchanged for the next 90 min. Consequently, despite the greatest increase in the quantity of edema fluid by the 30th minute after injection of the fatty acids, intensification of ventilation prevented the development of hypercapnia throughout the period of development of EL investigated.

Thus the use of enhanced parameters of AV during the development of edema of the lungs improved the gas exchange, reduced hypoxia, and prevented the appearance of hypercapnia. Under these circumstances, a greater effect as regards oxygenation of the blood was achieved by an increase in the frequency of AV than in its volume.

Increasing the gas exchange in the lungs with an increase in the frequency of volume of AV during the development of EL delayed the fall of the systemic BP (Fig. 2c) and increased the length of survival of the animal (Fig. 3). For instance, with the initial ventilation programs, of 14 animals studied toward the 90th minute after injection of fatty acids, four survived. By this time their BP had fallen from 102 ± 8 to 40 ± 12 mm Hg. The development of edema of the lungs accompanied by an increase in both frequency and volume of AV led to survival of 11-12 animals from the same number of those studied. By the 90th minute of edema, their BP was reduced only by 10-15% of its initial value.

To aggravate the process during the development of EL, physiological saline can be injected into the blood stream [6]. In the present investigation, intravenous injection of 3-4 ml of physiological saline during the development of EL, with the initial AV programs, led to death of all the animals in the course of 2-3 min, evidently on account of severe hypoxia. Against the background of an increase in the frequency or volume of AV, injection of the same quantity of fluid caused by a transient fall of BP by 15-20 mm Hg, and death of the animals did not occur once.

Consequently, by improving the gas exchange in the lungs and thereby restoring normal values of BP, an increase in the frequency or volume of AV increases the resistance of the animal to development of toxic EL, even during exacerbation of the process as a result of intravenous injection of fluid.

The development of EL in the experimental animals was accompanied by the excretion of frothy fluid from the lumen of the trachea. The frequency and time of its appearance depended on the conditions of AV (Fig. 3). With the initial AV progams, foam appeared in half of the animals studied on average 15 min after injection of the fatty acids. In all other cases frothing did not take place. The development of EL after an increase in the frequency of AV led to foam formation in only two, compared with five when the volume of AV

was increased, of the 15 animals. Under these circumstances, foam began to appear from the trachea during the development of EL, not earlier than 60 min after injection of the fatty acids. On the basis of the results and data in the literature [7, 12] on an increase in lymph drainage from the lungs when pulmonary ventilation is increased, it can be tentatively suggested that delay in the outflow of extravascular fluid into the lumen of the alveoli and of foam formation in experiments during the development of EL, accompanied by an increase in the frequency and volume of AV, is connected with stimulation of the pulmonary lymph drainage, as a result of which the pressure in the interstitial space falls and removal of toxic products, damaging the alveolar epithelium, from it is accelerated. Stimulation of lymph drainage during the development of EL may perhaps depend more on an increase in the frequency of respiratory movements than on an increase in alveolar pressure associated with an increase in the volume of AV, for an increase in the frequency of AV had the greatest effect on the reduction of foam formation in the present experiments.

It can be concluded from the results that the use of an increase in the frequency or volume of AV in toxic edema of the lungs delays the increase in the pulmonary coefficient and in the quantity of edema fluid in the initial stages of its development, and does not increase the degree of edema subsequently. It reduces frothing, increases the survival rate of the experimental animals, delays the fall of the systemic BP, and improves the pulmonary gas exchange, thus making it more beneficial than the usual program of ventilation. An increase in the frequency of AV has a more favorable effect than an increase in its volume on the reduction of frothing and improvement of the gas exchange in the lungs.

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