It must be pointed out that induction of synthesis of antibodies to neurotransmitters precedes the development of autoimmune responses to visceral TA.

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EFFECTIVENESS OF EXTRACORPOREAL MEMBRANE OXYGENATION IN ANIMALS WITH ACUTE RESPIRATORY FAILURE

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UDC 616.24-008.64-036.11-092.9-085.835-036.8-07

KEY WORDS: extracorporeal membrane oxygenation; acute respiratory failure; hemodynamics; oxygen transport.

Of all the pathophysiological aspects of the use of extracorporeal oxygenation in the combined treatment of acute respiratory failure when artificial ventilation of the lungs (AVL) proves ineffective, the greatest attention has been paid to gas exchange [2-5, 7, 9]. Changes in the circulatory system accompanying the method of extrapulmonary oxygenation, which are no less important in determining the oxygen supply to the body, have not been systematically studied, and fragmentary information on this matter can be found only in isolated publications [6, 8, 9].

The aim of the present investigation was to study the state of the central hemodynamics, gas exchange, and oxygen transport in animals with marked hypoventilation during the period of extracorporeal membrane oxygenation using different methods of perfusion.

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 7, pp. 12-14, July, 1986. Original article submitted June 14, 1985.

0007-4888/86/0007-0880$12.50

EXPERIMENTAL METHOD

Experiments were carried out on 13 anesthetized (trimeperidine 8 mg/kg, pentobarbital 10-15 mg/kg body weight), heparinized (2-3 mg/kg) dogs weighing 17-35 kg. Acute ventilation failure was produced by injection of muscle relaxants (suxamethonium 2 mg/kg) and by instituting AVL under severe hypoventilation conditions: 55.3 ± 2.8 ml/(kg•min). In the terminal stage of death from respiratory failure, which developed after 10-18 min, without changing the AVL conditions extracorporeal oxygenation was commenced, using the Soviet MOST-122 membrane oxygenator, included in an assisted circulation circuit with roller pump, intended for resuscitation purposes. The assisted circulation system was filled with polyglucin (800-900 ml). In six experiments veno-arterial perfusion was given for 2 h, and in seven other experiments veno-venous perfusion for 2-4 h (VAP and VVP, respectively). Blood entered the apparatus from the inferior vena cava through catheters introduced into the femoral veins, and oxygenated blood was injected during VAP into the femoral and axillary arteries, and during VVP into the external jugular vein. In the latter case VVP was preceded for 5 min by artificial veno-arterial circulation to restore the coronary circulation, raise the arterial pressure (BP), and prevent overloading of the right heart, as quickly as possible. During perfusion heparin was again injected (0.2-0.4 mg/kg•h) and, if necessary, suxamethonium (6 mg). Before the extracorporeal oxygenation was stopped the animals were switched to a normal program of AVL with 40% oxygen, which was given until adequate spontaneous respiration was restored. BP, the central venous pressure (CVP), and ECG were recorded during the experiments, the cardiac output was measured by the thermodilution method, and the acid-base balance and gas composition of the blood were determined. Tissue from the lungs and kidneys was taken from some animals 7-10 days after the experiments for morphologic analysis. The results were subjected to statistical analysis by nonparametric tests [1].

EXPERIMENTAL RESULTS

Before the beginning of extracorporeal oxygenation the animals developed an extreme degree of hypoxemia, hypercapnia, and uncompensated acidosis, superposed on hemoconcentration, i.e., the characteristic picture of death from mechanical asphyxia (Fig. 1: a-e). Membrane oxygenation, during the first 15-30 min of treatment, significantly increased HbO_2 and pO_2 and reduced pCO_2 in the animals' arterial blood (Fig. 1: a, b, e). However, these parameters did not regain their original values in the subsequent stages of perfusion and were somewhat better in the case of VVP than of VAP, despite the weaker extracorporeal flow: 59.0 ± 7 and 81.6 ± 5 ml/(kg•min), respectively. The changes observed in the blood-gas composition corresponded to the degree (and initially, to the rate also) of compensation of mixed acidosis (Fig. 1: c, d). The more marked hypoxemia and hypercapnia in the animals treated by VAP were the result of the irregular distribution of oxygenated blood in the body, for its greatest volume (three-quarters) was destined for the distal part of the animal.

The operation of the membrane oxygenator remained stable throughout the period of perfusion. The pCO_2 level of the blood fell after its passage through the oxygenator on average by 16.1 ± 1 mm Hg, and remained at a relatively high level (55.2 ± 1.4 mm Hg). The blood oxygen saturation, however, reached 95.0 ± 1.2%, an increase of 36.0 ± 2.0%.

The total systemic blood flow (equal to the cardiac output in the case of VVP, but equal to the sum of the cardiac output and the extracorporeal flow in the case of VAP) was virtually the same during extrapulmonary oxygenation in the two groups of experiments and showed a tendency to fall gradually. In the initial stages of perfusion it was 3-3.5 times higher than the initial values, and remained twice as high after 1 h (Fig. 1f). The total oxygen transport also was increased by 1.4-1.7 times during the first hour, and returned close to its initial value after 2-3 h (Fig. 1g). Consequenlty, the level of the systemic blood flow, whatever method of perfusion was used, compensated the negative effect of hypoxemia and hemodilution (the average hematocrit — HT — reaching was 32 ± 1%, compared with an initial value of 52 ± 2%), on total oxygen transport in the body. Reduction of the oxygen debt was reflected in a positive trend of the blood acid-base balance (Fig. 1: b, c, e). In the case of VAP by the scheme indicated above, however, because of disturbance of the natural distribution of arterial blood, it was not the systemic blood flow, but part of it — the cardiac output (CO) — which was most informative as regards the blood and oxygen supply to the proximal part of the body, including the brain and heart. In the experiments with VAP, CO exceeded the initial values (by 2-2.4 times) only during the first hour, and later it decreased (Fig. 1: f). Correspondingly the oxygen transport, dependent on CO, was maintained at the original level within the same time interval, but after 2 h it fell almost by half (Fig. 1g). Despite the generally satisfactory

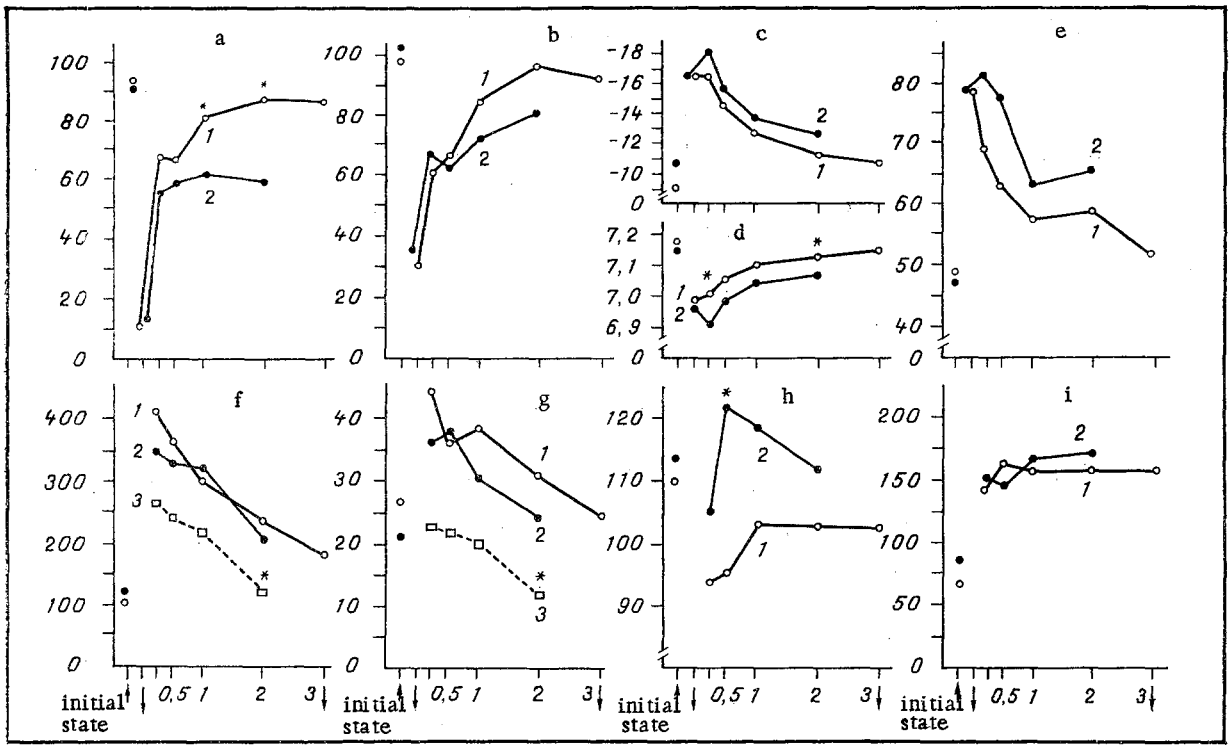

Fig. 1. Parameters of central hemodynamics, acid-base balance of arterial blood (from the axillary artery), and oxygen transport in animals with acute respiratory failure during extracorporeal membrane oxygenation. Abscissa, duration of oxygenation (in h). Arrow pointing upward — original value. Ordinate: a) degree of oxygen saturation of blood (in %); b) partial pressure of oxygen (in mm Hg); c) base deficit (in meq/liter); d) pH; e) pCO_2 (in mm Hg); continuous line represents systemic blood flow, broken line cardiac output (in ml/kg•min); f) continuous line — systemic blood flow, broken line — cardiac output (in ml/kg•min); g) continuous line — total oxygen transport, broken line — oxygen transport maintained by CO (in ml/kg•min); h) BP (in mm Hg); i) heart rate (beats/min). 1) VVP; 2, 3) VAP. Asterisk indicates statistically significant differences between groups (Mann—Wilcoxon—Whitney test).

level of oxygen transport, the oxygen supply to the proximal part of the body became inadequate and required special correction as perfusion continued. Possibly the worsening of the neurologic status, sometimes observed during prolonged veno-arterial membrane oxygenation [6], may be connected with this irregular change of the oxygen supply to individual organs. Consequently, during VAP, to maintain the optimal oxygen balance of the body as a whole, attention must be paid not only to the level of the extracorporeal flow and blood gas composition of the animals, but also to their CO.

The higher CO in the case of VVP than of VAP can be attributed to the increased venous return and the lower peripheral resistance. BP at all stages of the experiment was lower when VVP was used, whereas no significant differences between the groups were observed in the values of CVP and the severity of tachycardia (Fig. 1: h, i). With VVP the heart evidently worked under conditions of a more increased preload and reduced afterload.

Of seven animals undergoing veno-venous membrane oxygenation under conditions of very severe respiratory failure, five dogs survived with full restoration of CNS function: three of them had undergone perfusion for 3 h, two of them for 2 h. Of six animals undergoing veno-arterial oxygenation four were still alive after perfusion for 2 h. Hemolysis was absent in all the experiments. Death of the remaining animals (on the 1st-3rd day) was largely associated with excessive hemodilution (Ht 20-25%), which significantly limited the duration and abolished the positive effect of extracorporeal oxygenation.

Histologic investigation of the animals' lung tissues after perfusion by the two methods revealed solitary foci of microatelectasis, signs of mild interstitial edema, and regions with thickening of the alveolar septa. Occasionally sludging was found in the microcirculatory bed, and sometimes thrombi and mild plasma seepage through the vessel walls were observed. Evidence of cloudy swelling of the epithelium of the proximal tubules and mild interstitial edema was

noted in the kidneys. The mild nature and reversible character of most of the changes discovered point to preservation of functional homeostatis of the lungs and kidneys.

Under conditions of acute respiratory failure, extracorporeal oxygenation of the blood by the veno-venous method is thus preferable to the veno-arterial method as regards compensation of the gas-exchange function of the lungs, the working conditions of the heart (in the absence of cardiac decompensation and severe pulmonary hypertension), and maintenance of the oxygen transport in the body.

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EFFECT OF HYPOTHALAMIC ELECTRICAL STIMULATION ON PROTEIN SYNTHESIS IN ORGANS OF ADULT AND OLD RATS

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UDC 616.831.41-02:615.844]-07:616.1].4-008.939.6-092.9

KEY WORDS: protein synthesis; age; hypothalamus

In the modern view the mechanisms of aging at the organismal level are largely determined by age-related disturbances of hypothalamic function, but at the subcellular and cellular levels they are reflected in disturbances of regulation of genome expression [3]. Previously the writers discovered important age differences in the effect of hypothalamic electrical stimulation on transcription of different classes of RNA and induction of certain key enzymes in the rat liver [5].

Age differences in hypothalamic regulation of total protein synthesis in different organs and also of liver chromatin proteins were compared in the investigation described below.

EXPERIMENTAL METHOD

Adult (aged 11 months) and old (aged 23-24 months) Wistar rats were used. Electrical stimulation of the hypothalamus was applied on unrestrained animals by a bipolar technique between symmetrically placed electrodes, inserted into the medial hypothalamus 2-3 weeks before sacrifice of the rats, in accordance with coordinates of a sterotaxic atlas with corrections for age [5]. The parameters of stimulation were: a continuous series of pulses 1 msec in duration and with a frequency of 100 Hz, duration of stimulation 15 min. The strength

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 102, No. 7, pp. 14-16, July, 1986. Original article submitted May 25, 1985.