USE OF A MEMBRANE OXYGENATOR FOR MINOR PERFUSION TO CORRECT FUNCTIONAL SHIFTS ASSOCIATED WITH RESPIRATORY DISTURBANCES

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The effectiveness of assisted extracorporeal blood oxygenation (ECBO) for the correction of hypoxic states is largely determined by the method of connecting the membrane oxygenator (MO) to the patient or experimental animal [2, 4, 5]. That is why the choice of method of connection of MO which would be simple, readily available, and nontraumatic, is of the utmost importance for clinical practice. All these demands are satisfied by Seldinger's [7] method of connecting the extracorporeal system, as is used in hemodialysis and hemoperfusion. However, a number of problems arise in this case: Is the use of this technique justified in a different clinical situation, when ECBO is used for the treatment of hypoxia; how, when the rate of the blood flow through MO is limited, due to the introduction of thin catheters into the blood vessels by Seldinger's method, can adequate gas exchange be assured during ECBO; finally, what degree of hypoxia can be compensated by the use of perfusion with low volume velocities.

In this investigation the writers attempted to answer these questions in experiments on dogs with ventilation hypoxia and peripheral veno-venous connection of the "Sever-OMP" membrane oxygenator, with restricted blood flow through it.

EXPERIMENTAL METHOD

Experiments were carried out on 11 mongrel dogs of both sexes weighing 18-20 kg. After premedication with pentobarbital (20 mg/kg) the animals were given an intravenous injection of hexobarbital (10 mg/kg) every 60 min to maintain anesthesia. After muscle relaxation with succinylcholine (1 mg/kg at the beginning of the experiment and 0.3 mg/kg whenever signs of spontaneous breathing appeared), after intubation the animal was artificially ventilated by means of the RO-6 apparatus. Adequacy of ventilation was verified by measuring CO_2 and O_2 concentrations in the alveolar air and their partial pressure in arterial blood. Later the respiratory minute volume of the animal was reduced by 40-50%. Hypoventilation continued for 2 h. In the main series of experiments, ECBO was applied after hypoventilation for 10 min, whereas in the control series (4 experiments) it was not applied. In all experiments the animals were given heparin intravenously (10 mg/kg initially and 0.5 mg/kg every 30 min during perfusion). The MO was connected in accordance with the vein—oxygenator—vein method. The perfusion system consisted of the "Sever-OMP" MO (a description of its technical specification was given previously [1]), a receiver with a capacity of 150 ml, and a pump (the ISL-3 apparatus). Venous blood from the system of the inferior vena cava was collected through a catheter introduced into the left femoral vein. It gravitated into MO, which was placed 50-60 cm below the level of the animal's heart, and was returned from the receiver by means of a pump into the right atrium. The volume velocity of blood flow through MO was 14-17% of the cardiac output. The experiments were carried out under conditions of normothermia and hemodilution, and blood from donors was not used. The perfusion system was filled with Ringer's solution (400 ml), 5% glucose (200 ml), and rheopolyglucin (200 ml). Hemodilution was 30-40 ml/kg. The gas exchange in the animal's body and in MO was estimated from the values of the partial pressure of O_2 and CO_2 in

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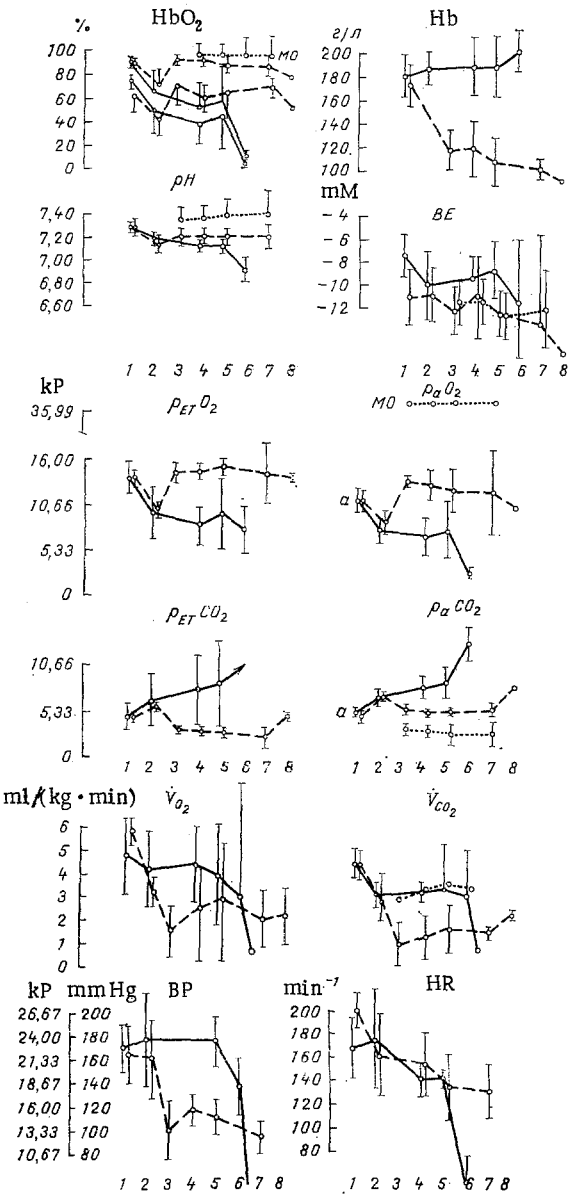

Fig. 1. Changes in parameters of gas exchange and hemodynamics during hypoventilation in control (continuous line) and with correction of disturbed respiration by small volumes of perfusion with MO (broken line). 1) Initial state (artificial normoventilation), 2, 4, 5, 6) after 10, 30, 60, and 90 min of hypoventilation respectively in control; 2, 3, 4, 5, 7, 8) after 10 min of hypoventilation and 10, 30, 60, and 120 min of ECBO against the background of hypoventilation, and 10 min after disconnection of MO with initial level of hypoventilation, respectively. $p_{ET}CO_2$, $p_{ET}O_2$) partial pressure of CO_2 and O_2 in end-expired (alveolar) air, Hb) blood hemoglobin concentration, pH) true pH of arterial blood, BE) base deficit in arterial blood, HbO_2) saturation of blood hemoglobin with oxygen; $\dot{V}O_2$ and $\dot{V}CO_2$) O_2 uptake in lungs and CO_2 excretion in lungs, and total (line of dots and dashes) uptake and excretion in lungs and MO; BP) maximal blood pressure, HR) heart rate, p_aO_2, p_aCO_2) partial pressure of O_2 and CO_2 in arterial blood.

alveolar and mixed expired air, the partial pressure of these gases and oxygen saturation of hemoglobin in arterial and venous blood, and the acid–base state (ABS). The respiratory minute volumes, and minute volumes of gas and blood passing through MO were determined simultaneously. On the basis of these data a number of calculated parameters of gaseous homeostasis of the animal were obtained. AME-1 analyzers, an OS M2 oxymeter (from Radiometer, Denmark), a Soviet MKh 6202 mass spectrometer, the general characteristics of which were given previously [3], and an RKÉ-2M blood flowmeter were used. The gas exchange was investigated after premedication and anesthesia during spontaneous breathing and AVL, after hypoventilation for 10, 30, 60, and 90 min, and before the animal's death, and in the experiments with ECBO, 10 min after hemodilution, after 10 min of hypoventilation, and 10, 30, 60, and 120 min after the beginning of connection of MO. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Actual results of the investigation are given in Fig. 1. In control experiments the selected level of artificial hypoventilation (RMV 60% of normal) caused hypoxemia and hypercapnia, and hypoxia, and metabolic and respiratory acidosis developed gradually. The animals died after 45-100 min (average 75 min).

In the main series of experiments preliminary hemodilution reduced the fraction of hemoglobin in the blood by volume, but had no significant effect on gaseous homeostasis. During hypoventilation for 10 min the parameters of gas exchange in the lungs changed in the same direction as the control, but not significantly. During ECBO, the disturbances which appeared did not progress, and some parameters improved. In particular, $p_{ET}O_2$, p_aCO_2, and p_aO_2 were restored to normal. The oxygen saturation of hemoglobin in the arterial blood rose to its initial level. The pH of the blood improved greatly on account of a fall in p_aCO_2. The blood pressure and heart rate stabilized at a lower level.

These positive changes developed against the background of a substantial change in the gas exchange in the lungs: Excretion of CO_2 from them was considerably reduced, and oxygen uptake was reduced by a lesser degree, whereas $\Delta a_{ET}pCO_2$ in most cases was increased. The relationships observed, due to entry of oxygenated blood free from CO_2 into the right heart, also were noted previously in studies of arteriovenous and venovenous ECBO [5, 6]. The special features of gas exchange arising during operation of MO probably have a considerable, but as yet insufficiently studied, influence on oxygen transport from the lungs. Research in this direction is continuing.

Despite the small volume of the blood flow through MO, the relative contribution of its gas exchange (especially CO_2) was considerable. Its total value, according to data for gas exchange in the lung and MO, although for obvious reasons lower than in the initial state, was maintained at a stable level throughout the experiment.

The tendency observed for the base deficit to increase was not unexpected, for pharmacological correction of the modified ABS was not carried out. Nevertheless, parameters characterizing the animal's state were able to be maintained at a safe level. Not only did the animals not die, but at the end of the experiment their spontaneous breathing and a satisfactory circulation had been restored.

Under general anesthesia and with low volume velocities of blood flow through MO (14-17% of cardiac output) it was thus possible to maintain the gas exchange at a safe level (in these experiments for up to 2 h), with considerable hypoventilation (a decrease in RMV to 60-50% of normal). Small-volume ECBO can be undertaken by Seldinger's atraumatic puncture method, which is comparatively easy to perform. This method of extrapulmonary assisted oxygenation can probably be used for the correction of functional shifts in other lung disorders also. In particular, the combined use of membrane oxygenation of the blood by minor perfusion and AVL is a promising technique when the effectiveness of the latter is substantially reduced. Such a combination means that it is possible to avoid AVL with the use of a high respiratory volume and inhalation of pure oxygen, which may be dangerous for some patients.

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STATE OF MUSCLE CONTRACTILITY IN CHRONIC DISTURBANCES OF NEUROMUSCULAR TRANSMISSION

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Ever-increasing attention is being paid in the study of muscle function, of fatigue, and of mechanisms of disturbance of the contractile act in various pathological states, to the objective testing of muscle contractility, based on the study of the evoked mechanical response of the muscle to indirect stimulation [2, 4-7]. Investigators have noted the informativeness of determination of the ability of the muscle to undergo staircase potentiation and post-tetanic potentiation (PTP) and twitch time. These parameters vary in the course of fatigue due to physical exercise [5, 7] and also in endocrine myopathies [11]. Analysis of the force of a muscle during a single contraction may be difficult because of the high variability of this parameter in normal subjects [4, 6]. The study of the time course of force of a single twitch (FST) of a muscle has shown that it may not only be reduced, but also increased under certain conditions. The paradoxical phenomenon of an increase in amplitude of a single evoked mechanical response of a muscle during denervation and its decrease during reinnervation has been associated with a relative increase in the quantity of sarcoplasmic reticulum in atrophied muscle fibers [9].

The aim of this investigation was to analyze changes in amplitude of the evoked mechanical response of the muscle during chronic reversible disturbances of neuromuscular transmission.

EXPERIMENTAL METHOD

Altogether 84 patients were studied in whom chronic disturbance of neuromuscular transmission was due to myasthenia, an autoimmune disease which, in the modern view, leads to a decrease in the number of acetylcholine receptors on the postsynaptic membrane [10]. The patients' ages varied from 16 to 67 years and the duration of the disease from 1 month to 15 years. In 64 patients treated with anticholinesterase drugs, these were withheld for at least 12 h before the investigation; 20 patients were not previously treated with anticholinesterase drugs. Repeated tests were carried out on 23 patients before and during glucocorticoid treatment, at intervals of 3-6 months for 1.5-2 years.

Control group consisted of 24 healthy subjects aged from 20 to 55 years and 4 patients with hypothyroidism aged from 24 to 50 years; the latter were tested before and during replacement therapy.

The tests were carried out on an ÉMG 4-03 electromyograph with dc amplification channel for recording muscular contractions. The work done by the opponens pollicis muscle when contracting under isometric conditions (initial stretching of the muscle 500 g) was recorded. Stimulation of the ulnar nerve in the region of the wrist with square pulses of current from 0.2 to 0.5 msec in duration and of supramaximal strength was applied. To record the mechani-

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