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LIFE SUPPORT BY OXYGEN BREATHING AFTER TOTAL BLOOD REPLACEMENT BY DEXTRAN

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Artificial hemodilution, or treatment of blood loss by transfusion with blood substitute, invariably leads to the development of acute anemic hypoxia. The problem arises of whether life can be supported with this degree of blood dilution, when so few erythrocytes remain in the blood stream that they cannot ensure the transfer of the necessary quantity of oxygen.

To answer this question, experiments were carried out with replacement of blood by dextran, a blood substitute which can maintain constancy of the circulating blood volume (CBV) for a long period of time. Under these circumstances an extreme degree of hemodilution was produced, with a hematocrit index of below 5. It was shown previously that if the hemoglobin concentration is below 2-3 g% [2] or the hematocrit index below 5 [4-6] death from anemic hypoxia takes place. In the present experiments, to overcome or alleviate the hypoxia, the animals breathed oxygen at normal barometric pressure.

EXPERIMENTAL METHOD

Sixteen cats (9 experimental and 7 control) were anesthetized with pentobarbital (30 mg/kg body weight, intramuscularly). Blood replacement by dextran was carried out by means of 2 or 3 fractional exchange transfusions. Blood was withdrawn from an artery and the blood substitute was injected intravenously at the same rate. With this method, 94-98% of the recipient's blood was replaced [1]. The cats were intubated: The experimental animals breathed pure oxygen and the control animals atmospheric air. The following parameters were determined in the experiment: the arterial blood pressure (BP) in the femoral artery, the central venous pressure (CVP) in the mouth of the posterior vena cava, the pulmonary ventilation and oxygen consumption by the method of Douglas and Haldane, the partial pressure of oxygen (pO_2) in arterial and venous blood, the CBV by means of ^{51}Cr-labeled erythrocytes, the hematocrit index, and hemoglobin concentration. The cardiac output (CO) was calculated by Fick's method and the arterio-venous (A-V) difference in O_2 concentration, total peripheral resistance (TPR), and coefficient of oxygen utilization were determined. The various parameters were determined before, immediately after, and 1, 2, and 4 h after exchange transfusion.

EXPERIMENTAL RESULTS

In both experimental and control animals the hematocrit index after exchange blood transfusion did not exceed 2-3 and the hemoglobin concentration was 2 g%. Under these conditions the animals of the control group died 10-15 min after the end of blood replacement whereas the experimental animals did not die before the end of the experiment, which lasted 8-9 h.

KEY WORDS: hemodilution; oxygen therapy; blood substitutes.

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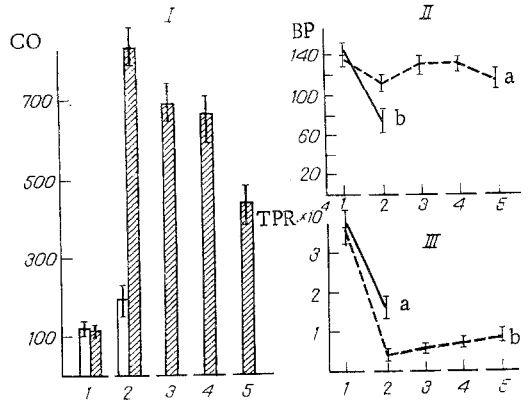

Fig. 1

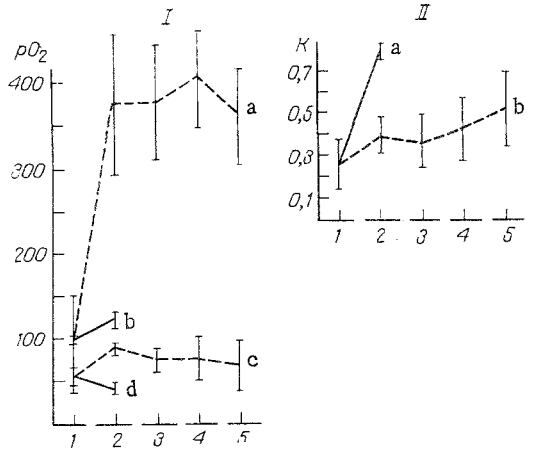

Fig. 2

Fig. 1. Principal hemodynamic indices during lethal hemodilution and oxygen breathing (M ± m). Abscissa, stages of experiment: 1) initial data; 2) immediately after blood replacement; 3) 1 h; 4) 2 h, 5) 4 h after blood replacement. I) CO (in $ml \cdot kg^{-1} \cdot min^{-1}$). Shaded columns — oxygen breathing; II) BP (in mm Hg): a) during oxygen breathing; b) during breathing atmospheric air; III) TPR (in $dynes \cdot cm \cdot sec^{-5}$): a) breathing atmospheric air; b) breathing oxygen.

Fig. 2. Partial pressure of oxygen in blood and coefficients of oxygen utilization in the presence of a lethal degree of hemodilution and during oxygen breathing. I) Partial pressure of oxygen in arterial (a, b) and venous (c, d) blood (in mm Hg): a, c) during oxygen breathing; b, d) breathing atmospheric air; II) coefficients of oxygen utilization: a) breathing atmospheric air; b) breathing oxygen. Remainder of legend as to Fig. 1.

What compensatory mechanisms supported life under these unusual conditions of the virtually complete absence of the animal's own blood? Let us examine the principal indices of the hemodynamics (Fig. 1). In the control animals BP and TPR fell steadily, but CO increased only by 1.5 times and could not even to a trivial degree have supported BP and compensated for the fall in TPR. Meanwhile in the experimental animals BP was maintained at a normal physiological level as a result of a marked increase in the cardiac output. CO in these animals immediately after exchange transfusion was almost 8 times greater than initially. There was a corresponding sharp decrease in TPR, which facilitated the work of the heart. CPV in both experimental and control groups was raised a little immediately after exchange transfusion, but later in the experimental animals it was quickly restored to its initial value.

When pure oxygen was breathed, the most important compensatory reaction was observed: an increase in CO maintaining the blood flow sufficiently to supply the tissues with oxygen. The fact that the oxygen demand was satisfied was shown by the stable level of oxygen consumption after blood replacement. Immediately after replacement it was 5.9 ± 0.8 $ml \cdot kg^{-1} \cdot min^{-1}$, after 1-2 h it was 6.9 ± 0.7 $ml \cdot kg^{-1} \cdot min^{-1}$, and after 4 h it was 6.5 ± 0.7 $ml \cdot kg^{-1} \cdot min^{-1}$ compared with an initial level of 4.9 ± 0.5 $ml \cdot kg^{-1} \cdot min^{-1}$. In control experiments the oxygen consumption immediately after replacement fell by more than half to only 2.1 ± 0.5 $ml \cdot kg^{-1} \cdot min^{-1}$ in the initial state. This severe degree of hypoxia was incompatible with life.

As a result of hemodilution the oxygen concentration in the artery immediately after replacement was only 1.4 ± 0.2 vol. % in the control and 1.9 ± 0.2 vol. % in the experiment. The contribution of physically dissolved oxygen in the control amounted to 0.3 vol. % and in the experiment to about 0.8 vol. %, and the remainder of the oxygen was combined with the hemoglobin of the residual erythrocytes. The oxygen concentration in the venous blood of the control animals was 0.3 vol. % (A-V difference 1.1 vol. %), whereas in the experimental animals it was 1.1 ± 0.2 vol. % (A-V difference 0.8 vol. %). How can such a negligible addition to the oxygen concentration (only 0.5 vol. %) maintain the necessary level of oxygen supply in the experimental animals? The main compensatory mechanism in this case was the high partial pressure of oxygen in the arterial blood (Fig. 2). During the first hours after replacement the partial pressure of oxygen was high in the venous blood also, and this prevented the

deoxygenation of hemoglobin, and at this time the erythrocytes did not take part in oxygen transfer. The high pressure gradient between artery and vein ensured a high diffusion pressure of oxygen from blood to tissue and, above all, to myocardial tissue. In control experiments, when the oxygen concentration in the blood was approximately the same but pO_2 was normal, the heart could not significantly increase its output. However, this compensatory mechanism can act only when the velocity of the blood flow is very high.

Diffusion of oxygen into tissues takes place not only in the radial, but also in the longitudinal direction, and the greater the blood flow, the slower the partial pressure of oxygen falls along the course of the capillaries in the tissue cylinder, the greater the longitudinal diffusion, and the more oxygen is supplied to the tissue. These facts can also be judged by a study of the coefficient of oxygen utilization, which showed a smaller increase in the experimental than in the control animals (Fig. 2).

An essential condition for the manifestation of these compensatory reactions described above is maintenance of the constancy of the CBV, as was secured in the present experiments, in which CBV was close to its initial level at all stages of measurement. This was done by administration of dextran, which maintains CBV more completely than any other blood substitute. Preservation of the constancy of the blood volume actually plays a more important role than preservation of its oxygen capacity. It was shown previously that breathing pure oxygen did not improve the oxygen supply to the myocardium and did not promote restoration of the hemodynamics after a considerable fall in CBV due to blood loss, although sufficient erythrocytes still remained in the blood stream [3]. Meanwhile if CBV was preserved, but in the almost complete absence of erythrocytes, oxygen breathing promoted the maintenance of cardiac function.

A high partial pressure of oxygen in the inspired air, a high velocity of blood flow, and a constant circulating blood volume, taken together, can support the animal's life for several hours after almost complete replacement of the blood by dextran.

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