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CHANGES IN OXYGEN SUPPLY LEVELS IN RATS AFTER EXCHANGE BLOOD TRANSFUSION WITH PERFLUORODECALIN EMULSION

Z. A. Chaplygina,* I. N. Kuznetsova,
V. S. Domracheva, N. Sh. Gokhman,
B. N. Maksimov, N. G. Panshina,
and I. G. Pankratova

UDC 615.384.015.4:612.26

KEY WORDS: blood gases; oxygen consumption; organofluorine emulsions; perfluorodecalin.

The creation of oxygen-transporting blood substitutes on the basis of organofluorine compounds (OFC) is attracting the attention of scientists in different countries [4]. The use of OFC for these purposes is dependent on their chemical inertness and increased ability to dissolve oxygen and other gases [11]. Usually OFC emulsions are studied on the whole organism or on isolated organs. However, the problem of the adequacy of the oxygen supply to the whole organism or to a perfused organ actually on account of the OFC emulsion is most frequently avoided and indirect indices are used in the calculation: the period of survival of the animals, the secretory function of the organ, and other indices [9, 10].

The object of the present investigation was to study the oxygen supply to the whole organism during exchange blood transfusion in rats with perfluorodecalin (PFD) emulsion. On the basis of these data the oxygen-transport properties of this medium can be assessed.

EXPERIMENTAL MATERIALS AND METHODS

Emulsions were obtained by an ultrasonic method using centrifugation to remove large particles. A 5% solution of a copolymer of ethylene oxide and propylene oxide, containing 0.15 M NaCl, was used as the emulsifier.

The PFD content in the emulsions was 20 ± 1 vol. %. The relative viscosity was lower than that of blood, namely 2.8 ± 0.5 cP; the concentration of the fluorine ion in the emulsions varied between limits of $0.6 \cdot 10^{-4}$ and $5.5 \cdot 10^{-4}$ M. The mean particle diameter in the different samples of PFD emulsions did not exceed 0.22-0.25 μ. The pH of the emulsions immediately before the beginning of the biological experiment was corrected by sodium bicarbonate solution to 7.4. The value of LD_{50} of the PFD emulsions was determined in experiments on albino mice and calculated by the method of Miller and Tainter [1].

Indices of the oxygen supply to the body were determined in acute experiments using a model of exchange blood transfusion in rats anesthetized intraperitoneally with sodium hydroxybutyrate (800 mg/kg) mixed with hexobarbital (40 mg/kg). Exchange transfusion was carried out by means of a hand-operated perfuser, pumping blood from the femoral artery and injecting emulsion synchronously into the femoral vein at the rate of 0.5-1 ml/min.

*Deceased.

Laboratory of Blood Substitutes, Leningrad Research Institute of Hematology and Blood Transfusion. (Presented by Academician of the Academy of Medical Sciences of the USSR V. N. Kulagin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 90, No. 11, pp. 546-548, November, 1980. Original article submitted January 28, 1980.

TABLE 1. Indices of Oxygen Supply of Rats after Exchange Blood Transfusion with PFD

Index	Before beginning of perfusion	After end of perfusion Ht = 10%
pO_2, mm Hg		
A	134 81—194	232* 159—389
V	34 23—47	30 17—56
pCO_2, mm Hg		
A	49 41—59	35* 24—48
V	64 53—73	69 40—93
Concentration O_2 (A), vols. %:		
mixed with Hb of blood	19,6 15,8—21,7	6,3* 2,7—8,0
dissolved	0,4 0,2—0,6	2,4* 1,6—3,1
CO, ml/min/g	0,30 0,22—0,47	0,40 0,19—0,48
O_2 consumption, ml/min/kg		
mixed with Hb of blood	34,0 22,9—51,3	12,9* 5,0—26,2
dissolved	0,8 0,5—1,1	6,7* 4,5—13,8

Legend. 1) Mean (M) and limits of variation of indices are given; n = 8. Data differing significantly from initial values indicated by asterisk.

The hematocrit index (Ht) was lowered to 10% or, in some experiments, to 5 and 1%, corresponding to a fall in the hemoglobin (Hb) concentration in the blood stream to 3.5, 2, and 0.5 g%, respectively. Before the exchange transfusion began the emulsion was oxygenated with moist oxygen for 20-30 min. In the course of the experiment the animals breathed moist oxygen spontaneously through a mask.

Before the beginning and after the end of perfusion the partial pressures of oxygen (pO_2) and carbon dioxide (pCO_2) in arterial (A) and venous (V) blood of the animals were determined on a Corning gas analyzer and the cardiac output (CO) also was measured by the thermodilution method. The oxygen capacity (OC) of the blood and perfusion medium and the oxygen consumption were calculated by the usual methods [2, 5]. During the calculations the coefficient of solubility of oxygen in PFD was taken to be 0.4 ml O_2/ml [11]. The degree of saturation of erythrocytic Hb with oxygen (HbO_2) in arterial blood was determined on an OS-1 oxyhemometer, and if Ht was below 10%, it was determined on the basis of the Hb dissociation curve and the value of pCO_2 (V).

EXPERIMENTAL RESULTS

LD_{50} of the PFD emulsion was 82.0 ± 2.9 ml/kg or, calculated as PFD itself, 30.8 g/kg. According to data of Clark [7] and Yokoyama [12], LD_{50} of emulsions based on PFD is 27 and 30.8 g/kg, respectively. LD_{50} of mixed Fluosol DA emulsion based on PFD (seven parts), and perfluorotripropylamine (three parts), calculated per total content of the OFC-phase, is 35 g/kg [13].

The initial OC of the test emulsion after saturation with oxygen was 10 vols.%.

The parameters of the oxygen supply to the body in the course of exchange blood transfusion in rats with PFD emulsion, at different stages of replacement, are given in Table 1 and Fig. 1: at Ht values of 10.5 and 1%. The total OC of the fluid circulating in the vessels at the end of perfusion was reduced at these dilutions by 2.5, 3, and 5 times, respectively. The relative contribution of dissolved oxygen to the total OC of the blood, mixed with emulsion, increased considerably and, at different degrees of replacement, it was 27, 76, and 90%, respectively. The decrease in the total OC after perfusion led to hyperventilation, as shown by a decrease in pCO_2 (A) and an increase in pO_2 (A) compared

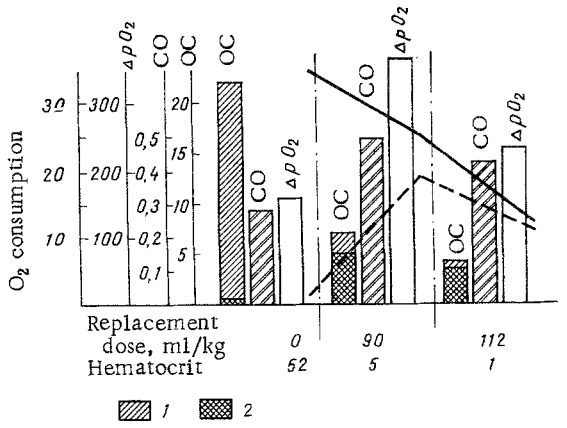

Fig. 1. Dynamics of oxygen supply to rats during exchange blood transfusion with PFD emulsion. Continuous line denotes change in total oxygen consumption, broken line change in consumption of physically dissolved oxygen from plasma (Ht 52%) and from PFD emulsion (Ht 5 and 1%). 1) Oxygen bound with Hb; 2) physically dissolved oxygen. Abscissa, stages of blood replacement. Ordinate, oxygen consumption (in ml/min/kg), gradient of partial pressure of oxygen ΔpO_2 (in mm Hg), CO (in ml/min/kg), OC of blood (in vol.%).

with initially. As replacement of blood by PFD emulsion continued the values of CO, which in the initial state was within normal physiological limits [3], increased: by 30% at Ht = 10%, and by 2 and 1.5 times, respectively, compared with the initial level at Ht values of 5 and 1%. This was evidently a compensatory reaction of the circulatory system to the fall in the total blood OC. Maintenance of the compensatory powers of the body in the presence of such considerable hemodilution was possible, most likely, because of the ability of the PFD emulsions to dissolve oxygen and because of the increase in the (A — V) pO_2 gradient compared with initially. According to the gas diffusion laws, an increased partial pressure of oxyben ought to provide improved conditions for the supply of oxygen to the tissues, including heart muscle [6].

The total oxygen consumption fell in the course of hemodilution. However, of the total quantity of oxygen used by the tissues, the dissolved part accounted for 34% when Ht was 10% and 76% when Ht was 5%. As Ht fell to 1%, dissolved oxygen accounted for 90% of the total quantity of oxygen used. Under these conditions the circulating emulsion provided only one-third of the oxygen consumed in the initial state. This could be due, first, to spontaneous elimination of particles of emulsion from the blood stream and, second, to the fact that the partial pressure of oxygen in the alveolar space was always below the level at which preliminary saturation of the emulsion with oxygen took place. For that reason the real OC of the emulsions *in vivo* must always be rather lower than their possible OC *in vitro*, and this also was observed in the present experiments.

Differential analysis of the oxygen-transport capacity of the PFD emulsion and of the erythrocytes remaining in the blood stream showed that the selected concentration of 20 vol.% is evidently optimal. Any further increase in the contribution of OFC to the emulsion would hardly be possible because of worsening of the rheologic properties of the OFC emulsions [8]. Lowering the concentration of OFC in the emulsion to 10-12 vol.% [10, 12, 13], however, does not appear to be justified because of the low OC of such preparations.

The oxygen supply to rats by PFD emulsion under certain conditions can thus attain values comparable with the initial level. In its biological properties — low toxicity and high ability to transport oxygen — PFD emulsion is a suitable medium for the creation of an "artificial blood" on its basis.

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EFFECT OF HYPOKINESIA ON NUCLEIC ACID AND PROTEIN METABOLISM IN CELLS OF RAT LYMPHOID ORGANS

G. S. Komolova

UDC 577.12+616-008.9

KEY WORDS: hypokinesia; nucleic acids; proteins; lymphoid organs.

One response of the body to hypokinesia is a reduction in weight of the lymphoid organs and in the number of lymphoid cells they contain [6]. During prolonged limitation of movement, biochemical changes also may take place in the cells of lymphoid organs [3, 4]. Lymphocytes are known to play an important role in the maintenance of homeostasis during prolonged exposure to stress under extremal conditions [1]. They have the functions of synthesis, storage, and transport of nucleoproteins, which can be assimilated by cells of other tissues.

The object of this investigation was to study the effect of hypokinesia on thymocytes and splenic lymphocytes with particular reference to nucleic acid and protein metabolism, for it is these parameters which mainly define the trephocyte function and humoral activity of lymphoid cells.

EXPERIMENTAL METHOD

Adult (about 80 days old) male Wistar rats, weighing 200-250 g at the beginning of the experiment, were used. Animals of the experimental and control groups were kept in the same room on a standard diet, but the experimental animals were kept in special restraint cages, greatly restricting their mobility. During the experiment, which lasted 22 days, the state of the animals was assessed periodically on the basis of their behavior, body weight, and blood picture. After decapitation of the animals their organs (thymus and spleen) were weighed, washed in cold physiological saline, and homogenized in a glass homogenizer with Teflon pestle. Cell suspensions were obtained by pressing the homogenates through Kapron tissue, and the stroma was removed. The cells were washed and suspended in medium No. 199. The thymocytes thus obtained were used for analysis immediately, and lymphoid cells were isolated from the spleen cell suspension by centrifugation in medium containing Ficoll and Verografin [10]. The number of lymphocytes was counted by the standard method in a Goryaev's chamber. The intensity of synthesis of DNA, RNA, and protein was determined from the rates of incorporation into their molecules of the corresponding

A. N. Bakh Institute of Biochemistry, Academy of Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Severin.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 90, No. 11, pp. 548-550, November, 1980.

 0007-4888/80/9011-1516$07.50