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PLASMA PROTEIN SPECTRUM OF DOGS TREATED FOR HYPOXIA WITH THE SEVER-OMR MEMBRANE OXYGENATOR

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KEY WORDS: hypoxia; membrane oxygenators; blood protein spectrum.

Membrane oxygenators (MO), instruments for nonpulmonary gas exchange, have become increasingly widely used for the treatment of hypoxic states in recent years. When their basic working parameters (gas-exchange properties) are studied, the need arises for assessment of the side effects of the foreign-body surfaces of the MO on the protein composition of the blood. Meanwhile, comparatively little is known about the character of the denaturation changes in blood plasma proteins due to prolonged operation of extracorporeal systems with MO [1, 6, 8]. It must be emphasized that the plasma protein spectrum of dogs — widely used experimental animals — obtained by electrophoresis on polyacrylamide gel (PAG) has received very little study.

The object of this investigation was to study the effect of the Sever-OMR MO on the blood protein spectrum of dogs during treatment for respiratory failure.

EXPERIMENTAL METHOD

Experiments were carried out on 12 mongrel dogs of both sexes weighing 18-22 kg, under morphine–hexobarbital anesthesia, using succinylcholine as muscle relaxant and artificial ventilation, under hypoventilation conditions (respiration rate 3-4 cycles/min, respiratory minute volume 40% of normal). For therapeutic purposes, for extrapulmonary additional gas exchange, the Sever-OMR MO was connected to an arteriovenous shunt formed on the femoral vessels. Artificial pumps were not used. The normal body temperature of the animals was maintained by an external heater. The volume velocity of the blood flow through the shunt was 800-1100 ml/min. The dose of heparin was 8-10 mg/kg (initial dose), followed by further injections of the anticoagulant under control of the activated blood clotting time.

The protein composition of the blood plasma was determined by electrophoresis on PAG [4] in blood samples taken from dogs in the initial state (after induction of anesthesia, during spontaneous respiration) and after prolonged (2.5-3 h) treatment for hypoventilation hypoxia by extrapulmonary gas exchange in the Sever-OMR MO. The data were analyzed visually and densitometrically (with a densitometer from Zeiss, East Germany, with attachment for a cylindrical gel). The number and relative position of the individual fractions were determined visually. The R_f values for each fraction relative to transferring, taken as 1, were determined from the densitogram.

EXPERIMENTAL RESULTS

By electrophoresis on PAG human blood plasma proteins can be divided into 20 or more fractions [4]. After partial or total denaturation of the protein molecule its quaternary

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TABLE 1. Coefficients of Migration and Number of Plasma Protein Fractions from Dogs under Normal Conditions and during Long-Term Oxygenation with the Sever-OMR MO (M ± m)

Protein fractions	R_f	Normal	Duration of action of MO, min	
			120	180
Albumins	1,77 ± 0,089	1,0 + 0,00	1,0 ± 0,00	1,0 ± 0,00
Postalbumins:	1,54 ± 0,063	1,5 + 0,24	1,6 ± 0,45	1,0 ± 0,00
fast	1,38 ± 0,035	2,6 ± 0,28	3,4 ± 0,30	3,3 ± 0,26
of average mobility	1,17 ± 0,021	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
slow	1,00 + 0,00	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
Transferrin				
Postransferrings:				
fast globulin	0,84 ± 0,014	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
globulins of average mobility	0,71 ± 0,06	1,1 ± 0,08	2,8 ± 0,20	3,0 + 0,08
slow glubulins	0,62 ± 0,036	2,1 ± 0,08	1,8 ± 0,17	2,0 ± 0,00
Immunoglobulins	0,39 ± 0,029	1,2 ± 0,16	1,0 ± 0,00	1,0 + 0,00
2nd start peak:				
macroglobulins	0,25 ± 0,01	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
lipoproteins	0,18 ± 0,005	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
1st start peak	0,04 + 0,01	1,0 ± 0,00	1,0 ± 0,00	1,0 ± 0,00
Total number of fractions		17 ± 0,4	18 ± 0,2	18 + 0,29

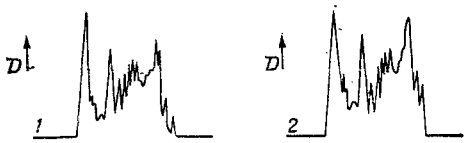

Fig. 1. Densitogram of dog's plasma protein spectrum: 1) normal, 2) after 2.5 h of parapulmonary oxygenation of blood during continuing hypoventilation.

structure, its molecular weight and charge and, as a result, its electrophoretic mobility are known to be disturbed. Accordingly, both the position and the intensity of the individual fraction on the gel are changed compared with normal, and the presence of denatured protein components leads to the appearance of additional peaks on the densitogram [7].

Because of the absence of data in the literature on interpretation of the plasma protein spectrum of dogs, individual electrophoretic zones were identified by analogy with spectra of human blood plasma proteins, which several investigators have studied [5, 7, 11].

Electrophoresis of plasma proteins from blood taken from the dogs before connection to the MO (normal) revealed rather fewer fractions than is characteristic of human blood: The prealbumin fraction was absent from all spectra. Beginning from the protein migration front in the electric field (Table 1) 12 electrophoretic zones could be distinguished, in the following order: 1) albumins, 2, 3, 4) postalbumins, 5) transferrin, 6, 7, 8) posttransferrins (globulins), 9) immunoglobulins 10) macroglobulins, 11, 12) two start peaks.

Individual differences in plasma protein spectra of healthy dogs were manifested as variations in the number of fractions of each zone; the greatest fluctuations were characteristic of the postalbumin fraction with average mobility and the fast postalbumin fraction (number of bands from 1 to 4).

In the writers' opinion, the best way to judge changes in the plasma protein spectrum during treatment of severe hypoxic states by means of an MO is on the basis of data obtained with arteriovenous connection of the oxygenator. Under these circumstances components of the extracorporeal system such as pumps, long communication pipes, heat exchange devices, and so on, do not affect the blood proteins. Another important feature is that by arteriovenous shunting of blood through the MO during hypoventilation a sufficiently high level of vital activity can be maintained in the animal for a long time and the hypoxia factor does not affect the blood proteins [2, 3].

The data in Table 1 reflect the number of protein fractions after connection of the MO to the animal for 3 h. Analysis of the data shows that the number of fractions in individual

zones as a rule does not increase, except in the zone of globulins with average mobility, where a slight tendency can be seen for the number of fractions to increase (the maximal range is 8%).

It will be clear from Fig. 1 that the two densitograms of the plasma protein spectrum from the same animal (before connection to MO and after its operation for 2.5 h) do not differ from each other significantly. It must be pointed out that even during very brief operation of bubble oxygenators considerable disturbances are observed in the composition of the plasma protein fractions, manifested as a change in electrophoretic mobility of individual fractions, with the disappearance of some and the appearance of the so-called extracorporeal circulation protein, which is absent under physiological conditions [9, 10].

It can be concluded on the basis of these data that during adequate perfusion and satisfactory compensation of hypoxia by means of the Sever-OMR MO for 3 h, the use of the oxygenator has no deleterious effect on the blood plasma proteins. Protein denaturation products — low-molecular-weight fragments of protein molecules — do not appear in the plasma during this period as a result of its contact with the surfaces of the fluoroplastic plates of the MO.

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COLONY-FORMING ACTIVITY OF STROMAL PRECURSORS OF BONE MARROW MECHANOCYTES IN LEUKEMIA AND HYPOPLASIA OF HEMATOPOIESIS

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KEY WORDS: fibroblast cultures of bone marrow; acute leukemia; idiopathic triple hypolasia of hematopoiesis; stromal precursors of bone marrow mechanocytes.

It has been suggested [4, 5] that the polypotent hematopoietic stem cell receives inducing information (determining the direction of differentiation) from adjacent stromal cells either by direct contact or through their microenvironment.

The most likely cells to transmit the inducing effect of the microenvironment are fibroblast precursors of stromal mechanocytes [2].

The method of obtaining discrete colonies of fibroblasts in monolayers by culturing a bone marrow cell suspension [1, 3] enables the state of the stromal precursors of the bone marrow mechanocytes or, in other words, the stromal microenvironment of the hematopoietic stem cells, to be assessed quantitatively.

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