OXYGEN SUPPLY OF THE ISOLATED RABBIT HEART DURING PERFUSION WITH ERYHEM (HEMOGLOBIN SOLUTION) AND BLOOD

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The coronary vessels of the isolated rabbit's heart were perfused with eryhem and diluted autologous blood; both solutions contained 2.5-3.0 g % hemoglobin. The oxygen capacity of eryhem, calculated per gram hemoglobin, is only 72% of the oxygen capacity of hemoglobin in red blood cells. Eryhem was shown to be capable of transporting and giving up oxygen. Meanwhile the oxygen supply to heart muscle perfused with eryhem was inferior to that of muscle perfused with blood. The necessary level of oxygen consumption was attained by increasing the coronary blood flow and utilizing more fully the oxygen reserves of the blood.
KEY WORDS: blood substitute; hemoglobin solution; isolated rabbit heart.

In several countries (USSR, Poland, USA, West Germany, etc.) research is in progress into the use of a solution of native hemoglobin (Hb) as a hemodynamic blood substitute, which at the same time is able to transport oxygen [1, 5, 7, 8, 10]. Whereas in the other countries investigations of Hb solutions as oxygen carriers are in the experimental stage, in the USSR the product eryhem, prepared by the Leningrad Institute of Hematology and Blood Transfusion, which contains about 3 g % Hb [6], is undergoing clinical trials. In view of the low oxygen capacity of eryhem, it is recommended as a stimulator of hemopoiesis and a hemostatic agent [1]. However, it is emphasized in a paper by Kolesnikov et al. [4] that the value of eryhem lies not only in its hemodynamic properties, but also in its ability to transport oxygen. Despite the detailed characteristics of eryhem now available, the problem of the extent to which it satisfies the oxygen demand of living tissues has not been studied by physiological methods.

To study this problem experiments were carried out on the isolated rabbit heart, whereby the ability of eryhem to combine with oxygen and to give it up to the tissues could be studied under pure experimental conditions.

EXPERIMENTAL METHOD

The heart was isolated by the method of Vishnevskii et al. [2], suggested for preserving the organ with a view to subsequent transplantation. Altogether five experiments in which the heart was perfused with eryhem and six in which it was perfused with autologous blood, diluted with physiological saline until the Hb concentration was 2.5-3 g %, were carried out. The isolated contracting heart was perfused by means of a resistograph under a constant perfusion pressure of 30-35 mm Hg. The perfusion fluid was pumped into the coronary arteries from the oxygenator and collected in the right ventricle, where it emerged from the coronary sinus, and also from the anterior cardiac veins of Thebesius. Through a special catheter, which served for the outflow of blood and for sample taking, the perfusion fluid passed into the oxygenator, where it was saturated with oxygen at atmospheric pressure, to $pO_2 = 159$ mm Hg. The temperature in the oxygenator and perfusion system was maintained at 38°C. Samples for analysis were taken at the outlet of the oxygenator (artery) and at the outlet of the right ventricle (vein). The heart rate (HR), volume of the coronary blood flow (CBF), concentration and partial pressure of oxygen (pO_2), partial pressure of carbon dioxide (pCO_2), the pH of the arterial (A) and venous (V) blood, and the oxygen capacity (OC) of the blood and eryhem solution were determined. The A − V difference of oxygen concentrations ($(A - V)O_2$), the degree of oxygen saturation (HbO_2) and oxygen capacity (OCHb) of 1 g hemoglobin of the blood and eryhem, and the oxygen demands of the heart muscle were calculated. All

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TABLE 1. Oxygen Supply of Myocardium during Perfusion of Isolated Heart with Diluted Blood (M ± m)

Index	Time from beginning of perfusion, min		
	10	30	60
Hb, g %	2,9±0,04	2,9±0,04	2,9±0,04
OC, vol. %	4,2±0,09	4,2±0,09	4,2±0,09
OCHb, vol. %	1,45±0,02	1,45±0,02	1,45±0,02
CaO_2, vol. %	4,1±0,18	3,9±0,2	3,9±0,2
CVO_2, vol. %	2,3±0,19	2,3±0,26	2,3±0,25
$(A-V)O_2$, vol. %	1,8±0,08	1,6±0,18	1,5±0,13
HbO_2, %	97±2,4	92±3,1	91±3,7
HbO_2 A, %	50±3,6	54±5,6	55±5,2
CBF, ml/min/100 g	98±7,1	96±6	74±12,1
O_2 consumption, ml/min/100 g	1,9±0,12	1,6±0,24	1,1±0,18
HR	148±14,9	140±14,8	119±22,3
pO_2 A, mm Hg	116±1,4	107±5,7	103±5,2
pO_2 V, mm Hg	45±3,5	49±2	51±1,9
pCO_2 A, mm Hg	7,6±1,1	6,9±0,8	7,6±1,5
pCO_2 V, mm Hg	10,4±1,2	9,7±1,3	9,9±2,1
pH A	7,22±0,06	7,19±0,06	7,13±0,06
pH B	7,10±0,05	7,09±0,05	7,05±0,07

TABLE 2. Oxygen Supply of Myocardium during Perfusion of Isolated Heart with Eryhem (M ± m)

Index	Time from beginning of perfusion, min		
	10	30	60
Hb, g %	2,6±0,03	2,6±0,03	2,6±0,03
OC, vol. %	2,7±0,05*	2,7±0,05*	2,6±0,08*
OCHb, vol. %	1,07±0,02*	1,07±0,02*	1,03±0,04*
CAO_2, vol. %	2,7±0,005*	2,6±0,03*	2,4±0,07*
CVO_2, vol. %	1,1±0,08*	1,1±0,14*	1,2±0,2*
$(A-V)O_2$, vol. %	1,6±0,06	1,5±0,14	1,3±0,2
HbO_2 A, %	99±1,6	95±1,4	92±1,1
HbO_2 V, %	39±2,8	39±4,7	44±5,6
CBF, ml/min/100 g	146±12,9*	144±10,3*	128±15,3*
O_2 consumption, ml/min/100 g	2,4±0,17*	2,2±0,23	1,6±0,27
HR	122±12,3	115±8,3	75±21,2
pO_2 A, mm Hg	113±5,8	105±4,3	88±2,6*
pO_2 V, mm Hg	21±1,4*	26±5,1*	30±4,5*
pCO_2 A, mm Hg	26±1,8*	30±3,5*	29±3,1*
pCO_2 V, mm Hg	46±3,3*	50±2,9*	51±7,8*
pH A	6,89±0,09*	6,78±0,1*	6,61±0,09*
pH B	6,76±0,08*	6,65±0,07*	6,50±0,07*

Legend. Data differing significantly from corresponding values in experiments with diluted blood ($V < 0.05$).

these indices were determined 10, 30, and 60 min after the beginning of perfusion.

EXPERIMENTAL RESULTS AND DISCUSSION

The main values characterizing the oxygen regime of the myocardium were: the oxygen concentration in the arterial blood and the level of Hb oxygen saturation, the oxygen concentration and degree of oxygen saturation of Hb in the system of the coronary veins, $(A-V)O_2$, pO_2 in the artery and vein, and the oxygen consumption of the heart muscle. It will be clear from Tables 1 and 2 that eryhem was sufficiently well saturated with oxygen, and the oxygen concentration, the Hb oxygen saturation, and pO_2 in eryhem corresponded to those in arterial blood. Not until the 60th minute of perfusion was pO_2 in eryhem substantially lower than in blood. This can be explained by the oxidation of eryhem (the formation of the met form) and some degree of denaturation of the protein, as confirmed by the results of appropriate investigations and data in the literature [3]. Eryhem

gave up oxygen to the tissues, and $(A - V)O_2$ for eryhem was equal to $(A - V)O_2$ for blood. Eryhem correspondingly satisfied the oxygen demand of the heart muscles.

However, maintenance of the necessary level of oxygen consumption by the heart during perfusion with eryhem and blood was achieved differently. In both cases the heart muscle received an inadequate oxygen supply and functioned under hypoxic conditions, but during perfusion with eryhem the hypoxia was more severe. This is clear from analysis of the venous blood. In the experiments with eryhem both the oxygen concentration and pO_2 were significantly lower than in the experiments with blood. Proof of the severe hypoxia was given by the more marked acidosis and the hypercapnia found in the eryhem solution flowing from the heart than in the blood.

The cause of the more marked hypoxia during perfusion of the heart with eryhem was its lower oxygen capacity than that of Hb contained in red blood cells. The oxygen capacity of diluted blood was in fact 1.4 vol. % higher than that of eryhem, although the Hb concentration in the blood was only 0.3 g % greater. This difference could be seen more clearly still when the oxygen capacity calculated per gram Hb was compared. For eryhem it was only 72% of the oxygen capacity of Hb in the red blood cells (Tables 1 and 2). The oxygen dissociation curve of eryhem also was shifted slightly to the left, interfering with the giving up of oxygen to the tissues [6, 9, 11].

For the compensation of anemic hypoxia under these experimental conditions the heart can call on two physiological mechanisms: vasodilatation (an increase in the blood flow) and the utilization of the oxygen reserves of the blood. Both of these mechanisms enabled the heart, in the experiments with eryhem, to maintain the necessary level of oxygen consumption.

The CBV was 50% greater during perfusion with eryhem than with blood; the relative bradycardia observed in the experiments with eryhem did not prevent the increase in CBF. The degree of utilization of the oxygen reserves of the blood was mentioned above. To satisfy the oxygen demand in the experiments with eryhem the heart utilized its reserves to a greater degree than in the experiments with diluted blood and, for that reason, the conditions of its oxygen supply were worse.

These experiments showed that eryhem can combine with oxygen, transport it, and give it up to the tissues. However, the concentration of eryhem investigated and the permissible dose for injection causing minimal changes in the organs prevent eryhem from being regarded as a blood substitute combined with oxygen carrier, for the quantity of oxygen carried by it is very small and cannot play a decisive role in the correction of oxygen insufficiency caused by blood loss or shock. An increase in the Hb concentration in eryhem would evidently enable it to be used as a perfusion medium for the preservation of isolated organs in vitro.

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