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EFFECT OF TEMPORARY HYPOVOLEMIA ON EARLY POSTRESUSCITATION CENTRALIZATION OF THE CIRCULATION AND SURVIVAL OF ANIMALS RECOVERING AFTER CLINICAL DEATH

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KEY WORDS: postresuscitation period; centralization of the circulation; hypovolemia.

The writers showed previously that centralization of the circulation takes place in the initial stage of the postresuscitation period, and that the intensity and duration of this response correlates postively with the severity of the state before recovery [1].

The aim of this investigation was to study the effect of temporary exclusion of part of the blood volume from the circulation on cardiac output, the distribution of its principal fractions, and the survival rate of animals recovering from clinical death.

TABLE 1. Cardiac Output and Its Principal Fractions in Postresuscitation Period (M ± m)

Parameter	Experimental conditions	Initial value	Postresuscitation period								
			min						h		
			3	5	10	15	20	30	1	2	3
CO, ml/kg	Experiment	140±7,3	140±15,3[c]	117±9,6[c]	91±8,8[a, c]	97±11,8[a,c]	110±11,5	115±13,5[b]	154±26,7	120±20,9	93±20,4[b]
	Control	162±9,3	264±17,9[a]	256±19,8[a]	203±28,7[b]	172±16,8	132±14,7	143±8,6[b]	139±8,9[b]	116±12,1[a]	100±9,8[a]
Supradiaphragmatic fraction, ml/(min·kg)	Experiment	70±9,3	86±12,8[c]	68±11,0[c]	50±9,9[c]	48±9,4[b, c]	58±11,4	58±8,8	90±19,5	43±8,6[a]	35±8,5[a]
	Control	77±6,3	168±16,7[a]	167±14,9[a]	119±19,5[b]	100±10,3[b]	72±10,6	73±7,9	62±6,1	47±6,5[a]	36±5,2[a]
Subdiaphragmatic fraction, ml/(min·kg)	Experiment	70±8,0	52±7,4[b, c]	49±6,8[c]	41±4,8[a, c]	49±4,6[a, c]	52±5,4[b]	57±7,8[bd]	64±12,9	77±12,9	58±12,2
	Control	85±5,3	96±10,5	89±8,3	84±13,3	72±9,5	60±6,4[a]	70±4,4[a]	77±6,2	69±7,1[b]	64±6,9[a]
CCC, units	Experiment	0,50±0,03	0,63±0,06[b]	0,58±0,07	0,54±0,09	0,49±0,06[d]	0,52±0,06	0,50±0,04	0,58±0,05[c]	0,36±0,02[a]	0,38±0,03[b]
	Control	0,47±0,02	0,64±0,03[a]	0,65±0,03[a]	0,59±0,04[a]	0,58±0,03[a]	0,54±0,03[b]	0,51±0,03	0,45±0,03	0,40±0,03[b]	0,36±0,03[a]

Legend. a) $P < 0.05$-0.001 (Student's test); b) $P \leq 0.05$-0.01 (Wilcoxon's test) compared with initial data; c) $P < 0.05$-0.001 (Student's test); d) $P \leq 0.05$-0.01 (Wilcoxon–Mann–Whitney test) compared with control.

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Fig. 1. Scheme of recording parameters of the hemodynamics. 1) Catheter transducer for measuring blood flow in inferior (posterior) vena cava; 2) thermistor for measuring cardiac output in arch of aorta.

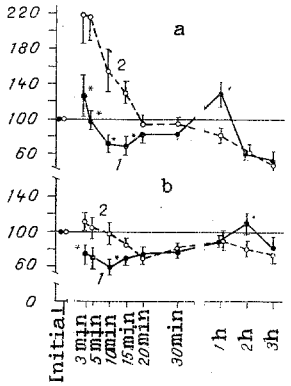

Fig. 2

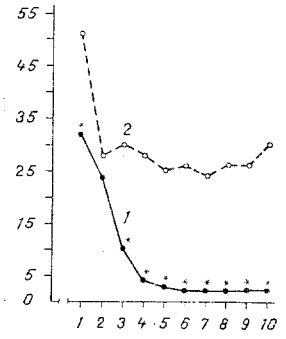

Fig. 3

Fig. 2. Supradiaphragmatic (a) and subdiaphragmatic (b) fractions of cardiac output in postresuscitation period (in % of initial – I). 1) Experiment (hypovolemia); 2) control. Here and in Fig. 3, asterisk indicates significant differences from control.

Fig. 3. Neurologic deficit (in points) in experimental (1) and control (2) animals in postresuscitation period. Abscissa – time (in days).

EXPERIMENTAL METHODS

Experiments were carried out on 42 cats of both sexes weighing 3.1 ± 0.1 kg, under pentobarbital anesthesia (40 mg/kg, intraperitoneally). Clinical death (5 min) was induced by arterial exsanguination. The experimental animals, after preliminary heparinization (500 U/kg), were subjected to hemorrhagic hypotension (Wiggers' model, 6.7 kPa, or 50 mm Hg, 30 min). Hypotension aggravated the course of the postresuscitation period, but at the same time, it enabled the animals to be resuscitated by intra-arterial injection of the lost blood and artificial respiration under moderate hyperventilation conditions (after Negovskii), without the use of any stimulants. The course of recovery was assessed by the usual tests

and by estimation of the neurologic deficit, using a modified 100-point scale [14]. The survival rate of the animals was determined from observations for 10 days. Temporary hypovolemia (30 min) was induced in the animals of the experimental group (19 cats) by Wiggers' method, by stabilization of the blood pressure (BP) at 13.3 kPa (100 mm Hg) immediately after resumption of effective cardiac contractions. The volume of blood transferred from the animal's vascular system into the reservoir was initially 20-25 ml/kg body weight. Later, as BP fell, blood was gradually returned to the vascular bed. If a small volume of blood remained in the reservoir after 30 min, it was invariably injected into the circulatory system. Animals (23 cats) in which the postresuscitation period followed its usual course served as the control. The distribution of the principal fractions of the cardiac output was studied by the method in [3]. For this purpose, the volume velocity of the blood flow in the thoracic portion of the inferior (posterior) vena cava was recorded by means of local thermodilution, and at the same time, the cardiac output (CO) was determined, also by thermodilution, in the arch of the aorta (Fig. 1). On the basis of the results the fraction of the cardiac output supplying blood to the anterior (supradiaphragmatic) segment of the body and the coefficient of centralization of the circulation (CCC) were calculated. This coefficient is the ratio of the supradiaphragmatic fraction to the total CO, and it can be used to estimate the response of centralization of the circulation at the systemic level [3]. The experimental results were subjected to statistical analysis by Student's test and by nonparametric tests.

EXPERIMENTAL RESULTS

Early results reflecting recovery of vital activity did not differ significantly in the control and experiment. Cardiac activity ws resumed on averaage after 1.1 ± 0.2 min, the first inspiration occurred 6.9 ± 0.6 min after the beginning of cardiac contraction, and the occular reflexes appeared after 19.5 ± 1.2 min.

The cardiac output in animals with hypovolemia did not increase in the postresuscitation period (Table 1). Moreover, after 10 min it was lower than initially and differed significantly from that in the control. The dynamics of distribution of the principal fractions differed significantly. Whereas in the control the blood flow in the supradiaphragmatic segment of the body was higher than initially for 15 min, under conditons of hypovolemia a small increase was not observed until the 3rd minute. Significant differences were found between the flow rates in the experiment and control before the 15th minute (Fig. 2). The blood flow in the subdiaphragmatic segments of the experimental animals in the initial stage of the postresuscitation period was less than in the control, and significantly lower than initially.

After reinfusion of the remaining blood the cardiac output increased somewhat until the 30th minute. The blood flow thereupon increased initially in the supradiaphragmatic segment (1 h), and later in the subdiaphragmatic segment (2 h). By the 3rd hour of the postresuscitation period the degree of the decrease in CO was about the same in the animals of both groups. Meanwhile the blood flow in the subdiaphragmatic segment remained at a relatively higher level in both experimental and control animals (83 ± 12 and 75 ± 8%, respectively) than in the supradiaphragmatic segment (50 ± 6 and 47 ± 5%, $P < 0.05$), i.e., decentralization of the circulation developed. CCC was significantly reduced 2 and 3 h after resuscitation.

The course of recovery and the survival rate differed in the experimental and control groups. The magnitude of the neurologic deficit in the control cats was significantly greater throughout the period of observation (Fig. 3). Of the 23 cats of the control group three survived, but only one with complete visible neurologic recovery, whereas of the 19 cats with temporary hypovolemia nine survived, seven of them with no neurologic deficit ($P < 0.05$).

Temporary exclusion of the path of the blood volume from the circulation in the initial stage of the postresuscitation period thus abolishes the phase of increase of cardiac output. The response of postresuscitation centralization of the circulation is weakened in intensity and shortened in duration, but most important of all, the blood flow is significantly reduced in the supradiaphragmatic segment of the body, most of which is assigned to the brain.

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EVALUATION OF THE ERYTHROPOIETIN-PRODUCING FUNCTION OF THE KIDNEY AND LIVER DURING CONTROLLED PERFUSION

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Erythropoietin (EP) is the specific hormone of erythropoiesis, the main source of which in man and animals is the kidneys [2, 4, 10]. During the study of erythropoiesis in animals after total and partial hepatectomy, combined with nephrectomy, it was shown that this hormone can also be synthesized by the liver, but in much smaller amounts than when the kidneys are present [10-12]. These findings indicate that the liver is the main source of extrarenal EP formation. In addition EP can be formed in other organs: the spleen, bone marrow stroma, stomach, pituitary gland, and hypothalamus [4, 9, 13]. During stimulation of erythropoiesis, increased EP formation takes place both in the kidneys and in the extrarenal sources. It is not yet clear (because of technical difficulties) what is the relative contribution of individual organs to the total balance of EP production under normal conditions and during intensive erythropoiesis [6, 8].

The aim of this investigation was a comparative study of the contribution of the kidneys and liver to total EP production in animals during excitation of erythropoiesis. For this purpose the method of perfusion of isolated organs (liver and kidneys) obtained from the same animal was used.

EXPERIMENTAL METHODS

Experiments were carried out on male mongrel dogs weighing 12-16 kg. EP formation was stimulated by the combined action of blood loss and injection of cobalt chloride. Blood equivalent to 25% of the blood volume was removed from the femoral vein of the animals 24 h

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