CHANGES IN SOME HEMODYNAMIC, ENDOCRINE, AND METABOLIC INDICES IN THE EARLY POSTRESUSCITATION PERIOD

A. V. Volkov, I. E. Trubina,
I. S. Novoderzhkina, L. V. Molchanova,
I. O. Zaks, and G. D. Savina

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Changes in the systemic circulation, the blood flow in the kidney and limb, and certain endocrine and metabolic indices were studied in 24 dogs subjected to circulatory arrest of maximal severity for 17 min in the course of 9 h of the postresuscitation period. Relative compensation and normalization of certain functions and metabolic indices during the first hour after resuscitation were subsequently followed by a new wave of disorders which developed at different times, unequally, and gradually in the body as a whole and in individual peripheral tissues. Disturbances of the peripheral circulation and central hemodynamics were shown to be among the leading pathological manifestations of postresuscitation sickness.

KEY WORDS: postresuscitation sickness; circulation; gas exchange; hormones; isozymes.

The leading role of hypoxic brain damage in the formation of irreversible changes in terminal states has now been established [2, 4, 5]. At the same time, the significance of some extracerebral factors in the development of illness in the resuscitated organism and, primarily, the question of hemodynamic provision for functions and metabolic processes in the body and in individual peripheral tissues after resuscitation still remain largely unexplained [1, 3, 6].

The object of this investigation was to study the central hemodynamics and circulation of the blood in the kidney, an important organ for the maintenance of homeostasis, and in the limb tissues, which are of considerable volume, and also to investigate certain endocrine and metabolic indices in the postresuscitation period after circulatory arrest lasting 17 min *in vivo*. This period of circulatory arrest was chosen, first, because it produces the severest form of hypoxia from which the early development of pathological changes can be expected, and second, on the basis of data in the literature [7] on the successful experimental treatment of this terminal state.

EXPERIMENTAL METHOD

Eighteen acute and six chronic experiments were carried out on 24 anesthetized (pantopon 8 mg/kg and pentobarbital 5-10 mg/kg) dogs. The animals were subjected to circulatory arrest for 17 min by induction of ventricular fibrillation by electric shock. The animals were resuscitated by external cardiac massage, intra-arterial infusion of physiological saline with adrenalin, electric defibrillation of the heart, and artificial ventilation of the lungs with oxygen [2, 5]. In the initial state and between 30 min and 9 h after resuscitation samples of arterial and mixed venous blood and of venous blood draining from the kidney and hind limb were taken in order to study the indices of the oxygen and acid–base balance and to determine the concentration of glucose by the toluidine blue method, of lactate by an enzymic method, of 17-hydroxycorticosteroids by the Silber–Porter reaction, to determine radioimmune insulin, and also to measure activity of lactate dehydrogenase (LD) and acid phosphatase (AP) and their isozymes [9, 10]. At the same time the total oxygen consumption, the cardiac output (by the Fick method), and the dynamics of the blood flow in the kidney and limb (by the hydrogen clearance method [8]) were studied and the systemic and pulmonary arterial pressures were recorded on a polygraph.

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TABLE 1. Changes in Hemodynamic Indices and Oxygen Balance in Early Postresuscitation Period

Stage of experiment	Statistical index	Central hemodynamics						Blood flow			O_2 consumption			Arteriovenous O_2 difference		
		CI, ml/min·kg	SI, ml/kg	pulse rate, beats/min	SAP, mm Hg	PAP, cm water	TPVR, dynes·sec·cm^{-5}	whole body	kidney	limb	whole body	kidney	limb	whole body	kidney	limb
								% of initial value			% of initial value			vols. %		
Before electric shock	M	156,5	1,47	118	104	17	3503	100	100	100	100	100	100	5,1	4,5	10,0
	$\pm m$	22,5	0,25	11,5	3,1	0,7	418,7							0,4	0,5	1,2
After resuscitation	n	17	17	17	17	15	17							17	16	15
30 min	M			185*	132*	25*			82,6†	123,1†		80,7†	55,5*		4,6	5,7*
	$\pm m$	—	—	8,9	9,6	3,2	—	—	9,8	12,5		10,8	7,6	—	0,6	1,1
	n			13	15	14			14	14		14	13		15	14
1 h	M	118,8	0,65*	180*	117*	18	4741	96,8	77,2*	113,8	128,7†	89,3	106,7	7,4*	5,1	9,3
	$\pm m$	18,2	0,08	5,6	2,8	2,2	525,9	19,5	7,6	21,7	15,5	33,1	31,3	0,6	0,9	1,1
	n	16	16	16	16	14	16	16	15	14	15	15	14	16	15	14
3 h	M	58,5*	0,39*	148*	111	15	8670*	46,1*	76,1*	73,3*	93,4	99,7	95,5	10,6*	6,3*	12,1
	$\pm m$	5,0	0,03	8,5	4,0	1,6	703,3	5,2	8,7	10,4	12,5	19,6	17,0	1,0	0,7	1,3
	n	16	16	16	16	15	16	16	13	12	14	12	12	16	13	14
6 h	M	75,5*	0,39*	190*	105	17	5546*	58,5†	57,7	57,3*	103,3	43,8*	72,2	9,2†	6,0	12,6
	$\pm m$	4,1	0,02	5,0	5,2	1,3	190,3	11,9	16,2	4,8	23,0	14,8	22,5	2,1	2,5	2,9
	n	3	3	4	3	3	3	3	3	3	3	3	3	4	4	4
9 h	M	74,1*	0,35*	207*	102	17	5379*	62,2†	55,3*	62,0	164,6	81,3*	76,8*	10,8*	6,4	12,5
	$\pm m$	3,3	0,01	10,0	6,9	1,4	222,7	15,9	8,9	20,3	44,1	4,5	5,6	1,0	1,4	1,4
	n	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3

*$P \leqslant 0.05$. †$P \leqslant 0.1$. Legend. CI) Cardiac index; SI) stroke index; SAP) systemic arterial pressure; PAP) pulmonary arterial pressure; TPVR) total peripheral vascular resistance. Here and in Table 2 P calculated relative to initial value.

EXPERIMENTAL RESULTS

Two periods are distinguished [4] in the changes in the indices determining the hemodynamic and endocrine-metabolic situation in the body during the first 9 h after resuscitation: The first (lasting 30-60 min after the beginning of resuscitation), characterized by resumption of functions and metabolism severely disturbed as a result of hypoxia, in its initial stage, followed by a tendency toward their partial compensation, and the second (1-9 h), characterized by the development of postresuscitation sickness.

Lasting cardiac activity was restored in the animals 2.9 ± 0.1 min, respiration 4.1 ± 1.2 min, and corneal reflexes 26.0 ± 0.6 min after the beginning of resuscitation. Despite the fairly rapid initial recovery at these times, profound disturbances of metabolism and the peripheral circulation were discovered in the first period (Tables 1 and 2). Severe metabolic acidosis developed with an increase in the lactate concentration in arterial blood to 483% of its initial level. LD activity was increased by more than 5-9 times and the relative proportion of activity of isozymes LD_{3+4+5} increased from 36 to 58%, evidence that enzymes were leaving the tissues for the blood. Posthypoxic hyperglycemia was slight, with a maximal increase in the blood glucose concentration to 176% of its initial level 1 h after the beginning of resuscitation. The total plasma insulin concentration fell by 60%. Blood AP activity was increased by 2.6 times, mainly on account of organ-specific AP isozymes not normally present and not inhibited by sodium tartrate. This was the result of activation of lysosomal enzymes in the tissues and of disturbances of permeability of the lysosomal and cell membranes.

The volume velocity of the blood flow in the limb tissues at the 30th minute of resuscitation was increased to 123% but the oxygen consumption was reduced to 55.5% of the initial level. At this time in the kidneys a similar increase in blood flow and decrease in oxygen consumption were found in five of the 14 experiments. In the other nine experiments the blood flow in the kidney was reduced to 58.3% whereas the oxygen consumption remained close to its initial level. Posthypoxic hyperperfusion in the limb in some experiments was not accompanied by abolition of the oxygen debt in the kidney, evidently because of shunting of the blood flow and disorders of the microcirculation [1, 3, 5].

The minute volume of the heart 1 h after resuscitation was close to its original level and the oxygen consumption of the whole body was increased by 28.7%. The blood flow and oxygen consumption of the limb tissues did not differ significantly from their initial values.

TABLE 2. Changes in Endocrine and Metabolic Indices in Early Postresuscitation Period (M ± m)

Stage of experiment	pH			BE, meq/liter		Lactate (artery), mg %	LD artery
	artery	renal vein	femoral vein	renal vein	femoral vein		total activity, milliunits/ml
Before electric shock	7,26±0,01	7,23±0,01	7,19±0,01	—9,5±0,5	—11,0±0,9	13,1±1,9	125±33
After resuscitation							
30 min	7,10±0,03*	7,03±0,04*	7,01±0,04*	—21,7±1,5*	—21,9±1,4*	66,8±8,0*	693±122*
1 h	7,13±0,03*	7,10±0,05*	7,05±0,03*	—19,6±2,2*	—20,5±1,6*	58,4±4,8*	1139±355*
3 h	7,23±0,02	7,16±0,02*	7,14±0,02*	—14,2±1,1*	—16,8±0,8*	35,6±4,5*	841±259
6 h	7,29±0,03	7,24±0,03	7,18±0,03	—11,1±2,0	—12,3±0,9	—	806±183*
9 h	7,29±0,03	7,24±0,03	7,15±0,02†	—11,7±1,6	—14,9±1,0*	—	503±20*

Table 2. (Continued)

LD	AP artery		Glucose (artery), mg%	Insulin, microunits/ml			17-hydroxycorticosteroids, μg %	
% 3+4+5	total activity milliunits/ml	% organ-specific		artery	renal vein	femoral vein	artery	renal vein
36	2,6±1,2	0	45,7±3,2	8,9±2,6	8,4±2,1	9,8±1,8	12,2±1,6	12,0±1,2
58	7,4±1,1*	41	77,2±9,4*	3,9±0,8*	3,6±0,8*	3,8±0,8*	—	—
52	6,9±5,7	28	80,5±10,0*	3,1±0,3*	3,7±0,7*	3,8±0,6*	—	—
51	13,7±4,1*	62	62,3±10,6	15,3±7,3*	10,7±4,5†	16,5±8,4*	15,4±0,8	13,9±1,1
42	14,2±5,2*	52	—	—	—	—	—	—
34	7,5±4,0*	16	—	—	—	—	—	—

*P ≤ 0.05
†P ≤ 0.1

The blood flow in the kidney was reduced by 22.8% and the oxygen consumption was close to its initial level. A tendency was found for the glucose consumption by the kidney and limb tissues to be increased. The results indicated changes in the normal distribution of the blood flows and volumes in the body during the first hour after resuscitation and differences in the character of the initial processes of recovery of metabolism in different tissues.

In the second period (1-9 h), besides a tendency toward normalization of individual disturbances, new pathological disturbances began to appear. The principal disturbance of this kind was a deficiency of hemodynamic provision for functions and metabolism. For instance, toward 3 h after the beginning of resuscitation the cardiac output fell to 46.1% and the stroke volume to 26.5% whereas the peripheral vascular resistance increased to 247.4% of the original value. The systemic and pulmonary arterial pressures showed no significant change. After 6-9 h the hemodynamic indices remained at the same level as after 3 h. The whole-body oxygen consumption remained close to its original level, the metabolic acidosis in the arterial blood was compensated, and the lactacidosis and LD activity in the blood were a little reduced, although they were still higher than initially by 172 and 302-573% respectively. A tendency was observed for the plasma glucocorticoid and insulin clearance of the kidney to increase. Besides the positive compensatory reactions noted above, pathological changes also developed. For instance, marked hyperinsulinemia and a fall in the blood glucose concentration were observed; the plasma 17-hydroxycorticosteroid concentration was low 3 h after resuscitation and indistinguishable from initially; activity of AP and its organ-specific isozymes was increased even more than in the first period (by more than five times compared with the initial level).

The blood flow and oxygen consumption of the limb and kidney tissues were reduced 3 h after resuscitation and the decrease in the blood flow in these organs was considerably less marked than the decrease in cardiac output. This fact suggested that at this time more profound disturbances of the circulation were present in other tissues. Not until 6-9 h after resuscitation was the degree of depression of the blood flow the same in the body as a whole and in the regions studied. After 3-9 h a tendency was found for pH to fall and the base deficit to increase during passage of the blood through the limb, and to a lesser degree through the kidney, as a manifestation of secondary hypoxia of these tissues.

Analysis of these results shows that after resuscitation the tissues of the limb and kidneys and also, judging from indirect evidence (changes in the glucose and insulin levels, in the activity of organ-specific AP and LD, and so on), evidently, the tissues of the splanchnic region also were under conditions of inadequate perfusion. This prevented recovery of the normal functions and created the conditions for gradual development of a secondary wave of hypoxia and the formation of irreversible changes initially in some tissues and later in the body as a whole, which ultimately led to death of all the animals after 24-48 h in the chronic experiments.

Posthypoxic changes in the peripheral circulation and central hemodynamics are thus numbered among the serious pathological manifestations of postresuscitation sickness which prevent the adequate course of protective and compensatory processes and may be the immediate cause of a contributory factor in the development of all the known complications of the postresuscitation period.

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