Course of Shock in Rats with Different Resistance to Shockogenic Trauma during Crush Syndrome

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Experiments on narcotized rats with crush syndrome showed that low resistant animals developed pronounced hypovolemia, hemoconcentration, blood hyperviscosity, impairment of oxygen metabolism, and central and peripheral hemodynamic disturbances, whereas in highly resistant rats the hemodynamics and oxygen supply to tissues were maintained at a sufficient level, while hemoconcentration and the increase in blood viscosity were less pronounced.

Key Words: *crush syndrome; rheology; hemodynamics*

In most studies of hemodynamic parameters the experimental data are averaged and the differences in the individual animal resistance to shockogenic factors are ignored. At the same time, experimental animals have different individual resistance to acute blood loss and hypoxia [3,4]. In animals with different resistance, phases of shock induced by the same factors are shifted in time. Analysis of this temporally irregular process by averaged data leads to misinterpretation of experimental results, and finally to low efficiency of unified approaches to the therapy of shock [5]. The mechanisms underlying adaptive and pathological reactions of animals with different resistance of the cardiovascular system to etiologically different shocks are poorly understood.

Here we studied the course of shock accompanying crush injury in animals with different resistance to shockogenic traumas.

MATERIALS AND METHODS

Experiments were performed on 35 male outbred rats weighing 370-400 g. Twenty rats were intraperitoneally anesthetized with 50 mg/kg thiopental and crush syndrome was modeled by 6-h compression of soft tissues on the thigh [6]. The heart rate (HR), systemic blood pressure in the femoral artery, and central venous pressure in the caudal vena cava at the level of the heart were recorded in intact and experimental rats 18 h after decompression. Cardiac output (CO) was estimated by the method of thermodilution. The stroke index, total peripheral resistance (TPR), systemic oxygen transport, total oxygen consumption (TOC), and circulation time were calculated routinely [9]. Blood gases, pH, and the main parameters of the acid-base equilibrium, including the contents of actual bicarbonate (HCO_3), total CO_2, and standard bicarbonate (SBC) and actual base excess (ABE), were measured in samples of mixed venous and arterial blood on an ABL-4 gas analyzer. Hematocrit was estimated by centrifugation. Viscosity of the plasma and whole arterial blood was measured on an AKP-2 rotational viscometer at shear rates of 10, 100, and 300 sec^{-1}. Erythrocyte aggregation was analyzed by syllectometry (half-aggregation period, $T^1/_2$) [8]. The erythrocyte deformability index was estimated by ectacytometry [2]. For evaluation of the rectum-skin temperature gradient, the rectal temperature was measured in the rectum with a mercury thermometer and skin temperature was measured by a temperature-sensitive resistor, whose tip was introduced under the right forelimb skin through a small cut near the shoulder.

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Blood coagulation was prevented by intravenous injection of 500 U/kg heparin. The animals were killed by narcotic overdose.

The results were analyzed by Statistica for Windows 4.3 software.

RESULTS

In the experimental group 20% animals died within 18 h after decompression. These animals were probably low resistant to shockogenic trauma. However, previous studies showed that 40% rats are characterized by low resistance to shock [5]. In low resistant rats shock is not followed by the compensatory phase and is characterized by rapid development of terminal stages (lifespan in these animals 2-fold shorter than in highly resistant rats) [5,9]. It was shown that the lifespans of low and highly resistant rats after crush injury are 30 and 58 h, respectively [7]. These data suggest that low resistant animals survived 24 h after trauma were in the terminal phase of shock, while highly resistant rats were in the phase of adaptation. Previous experiments demonstrated different relationships between parameters of systemic hemodynamics in the compensatory and terminal phases of traumatic shock [9]. This primarily concerns the CO-circulation volume (CV) and TPR—CV ratios at various stages of shock. A comparison of hemodynamic parameters in experimental and control rats allowed us to divide them into groups with high and low resistance to shockogenic trauma (as estimated by the TPR—CV ratio, Fig. 1).

Hemodynamic changes in highly resistant animals included hypovolemia, hypotension, and a 29% decrease in CO, which was related to reduced stroke volume (Table 1). Low arterial Po_2 and hypocapnia associated with hyperventilation and decreased pulmonary blood flow rate attested to disturbed gas exchange disturbances in the lungs. Blood hyperviscosity included intensive erythrocyte aggregation, decreased deformability index, and increased blood viscosity at various shear rates. These changes and decreased CO led to abnormalities in systemic oxygen transport. Impaired oxygen supply to tissues and microcirculatory disturbances associated with blood hyperviscosity were followed by a decrease in TOC to 44% of the control level (Table 1).

In low resistant animals we found a decrease in the stroke index and CO (26 and 23% of the control, respectively), bradycardia, hypoxemia, and disturbances in systemic oxygen transport (19% of the control). Low resistant animals were characterized by high hematocrit and plasma viscosity and decreased deformability of erythrocytes. Blood viscosity increased at various shear rates (10-300 sec^{-1}). CV in these rats was extremely low (51% of the control). These changes attested to the development of severe hemoconcentration and blood hyperviscosity. Rheological changes and pronounced hypovolemia led to peripheral circulatory disturbances. In low resistant rats the rectum-skin temperature gradient increased to a greater extent than in highly resistant animals (Table 1). Rheological and hemodynamic disturbances caused severe circulatory insufficiency and tissue hypoxia, which was confirmed by a 3.4-fold increase in the circulation time and decrease in venous blood Po_2 and TOC (by 4.6 times compared to the control, Table 1). The glomerular filtration rates in low and highly resistant rats decreased by 6 and 1.6 times compared to the control, respectively. This also indicated the development of severe hemodynamic disturbances in low resistant animals [10].

We found a paradoxical increase in TPR in low resistant rats. Previous studies showed that the terminal phase of shock is characterized by vasoplegia. At the same time, the contribution of vascular tone variations into TPR decreases during severe shock, while the role of blood viscosity increases [9]. Our previous studies revealed a correlation between TPR and blood viscosity at various shear rates in rats with the crush syndrome [12]. Experiments of S. A. Seleznev *et al*. demonstrated a relationship between blood viscosity and TPR during traumatic shock [9]. Therefore, the increase in TPR in low resistant rats is related to pronounced blood hyperviscosity.

All animals with the crush syndrome were characterized by blood alkalosis. However, changes in the acid-base equilibrium differed in highly and low resistant rats. In highly resistant animals we revealed an increase in SBC content and ABE and a decrease in

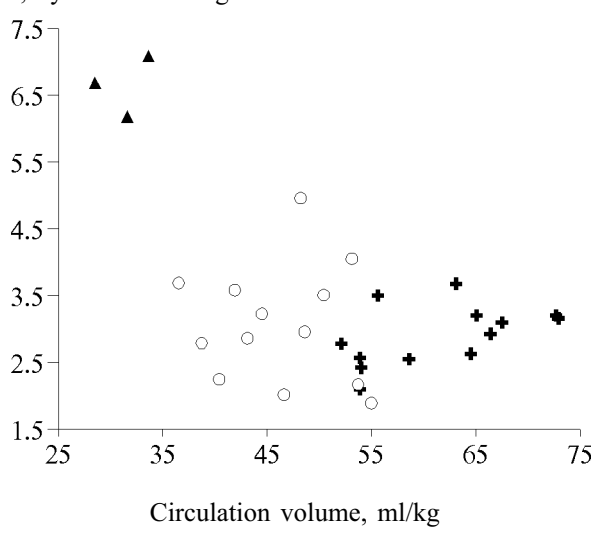

Fig. 1. Dependence of total peripheral resistance (TPR) on the circulation volume in intact (daggers) and highly (circles) and low resistant rats (triangles).

TABLE 1. Test Parameters in Low and Highly Resistant Rats with Shock Related to Crush Syndrome

Parameter		Intact	Shock	
			low resistant	highly resistant
TPR, dyn×sec×cm^{-5}×kg		2.85±0.12	6.69±0.69^{+}	3.07±0.25*
CO, ml/min/kg		339.4±16.5	79.1±18.5^{+}	240.8±15.8*$^{+}$
Stroke index, ml/m^2		0.84±0.04	0.22±0.04^{+}	0.61±0.03^{+}*
HR, bpm		412±9	340±20^{+}	397±13*
Systemic arterial pressure, mm Hg		123±9	63±16^{+}	86±5^{+}
Central venous pressure, mm Hg		15±2	4±6	13±1
CV, ml/kg		61.33±2.24	31.04±1.49^{+}	46.24±2.80*$^{+}$
Systemic oxygen transport, ml/min/kg		68.68±3.91	13.00±0.29^{+}	51.99±3.20*$^{+}$
TOC, ml/min/kg		23.30±1.95	5.04±0.09^{+}	10.25±0.61^{+}
Circulation time, min		0.17±0.01	0.58±0.10^{+}	0.20±0.01*$^{+}$
Rectum-skin temperature gradient, °C		5.0±0.4	8.9±0.1^{+}	8.00±0.02*$^{+}$
Po_2, mm Hg	arterial	87.7±3.3	72.8±4.0^{+}	79.7±1.9^{+}
	venous	34.8±2.5	28.1±1.6^{+}	36.8±1.0*
Pco_2, mm Hg	arterial	44.8±1.9	31.6±1.2^{+}	38.7±2.1*$^{+}$
	venous	55.3±2.0	47.0±3.3^{+}	49.2±2.1^{+}
pH	arterial	7.408±0.018	7.540±0.022^{+}	7.462±0.020*
	venous	7.357±0.013	7.408±0.019^{+}	7.403±0.013
HCO_3, mM/liter		27.8±0.2	27.6±2.1	29.1±1.3
Total CO_2, mM/liter		29.7±0.4	28.5±2.4	30.4±1.4
ABE, mM/liter		2.5±0.5	-0.9±0.9^{+}	4.4±0.8*
SBC, mM/liter		27.1±0.5	27.4±0.4	28.6±0.6^{+}
Hematocrit, %		46±1	63±1^{+}	50±1 *$^{+}$
$T^1/_2$, sec		10.3±1.3	2.1±0.1^{+}	2.2±0.1^{+}
Plasma viscosity, sPs		1.50±0.03	2.10±0.03^{+}	1.80±0.04*$^{+}$
Erythrocyte deformability index, rel. U		0.244±0.009	0.170±0.001^{+}	0.195±0.007*$^{+}$
Blood viscosity, sPs, shear rates, sec^{-1}				
	300	4.1±0.1	9.8±0.5^{+}	5.4±0.3*$^{+}$
	100	4.8±0.1	11.1±0.5^{+}	7.0±1.0*$^{+}$
	10	9.5±0.3	22.7±0.9^{+}	13.8±0.9*$^{+}$

Note. $p<0.05$: *compared to low resistant rats; $^{+}$compared to intact animals. The contents of HCO_3 and total CO_2, ABE, and SBC are measured in arterial blood.

Pco_2 (respiratory and metabolic alkaloses). These changes indicated the development of extracellular alkalosis, *i.e.*, blood alkalosis and tissue acidosis promoting hyperventilation. Intracellular acidosis results from a decreased volume of extracellular fluid or intracellular potassium deficiency, which is typical of rats with crush syndrome. In these animals potassium concentration in the heart and skeletal muscles decreased by 21-52%, while sodium content in skeletal muscles, liver, and kidneys increased by 17-61% compared to the control [1].

Progressive hypocapnia aggravated the symptoms of tissue hypoxia in low resistant animals. SBC content increased in highly resistant rats, but decreased to the baseline in low resistant animals. In rats with pronounced blood alkalosis ABE became a negative, which indicated accumulation of excessive nonvolatile acids in the blood and development of respiratory alkalosis. Previous studies showed that crush injuries in low resistant rats are accompanied by activation of anaerobic glycolysis and increase in blood levels of lactate, pyruvate, and inorganic phosphate by 3.9, 1.6, and 6.6 times, respectively, compared to intact animals. In highly resistant rats the contents of lactate and inorganic phosphate increased by 1.8 and 2 times, respectively. Thus, in low resistant rats pronounced lac-

tacidosis developed with the progression of respiratory alkalosis.

Our results indicate that in low resistant animals vasoconstriction is not the adaptive reaction directed to the maintenance of central hemodynamics. This is rather a pathological process accompanied by early ischemic damages to tissues, oxygen deficiency, lactacidosis, rapid loss of blood fluid, hemoconcentration, pronounced rheological disturbances, decrease in CV, and severe circulatory insufficiency. These changes cause death of low resistant animals. In highly resistant rats variations in the vascular tone, hemoconcentration, and increase in blood viscosity are less pronounced than in low resistant animals. Therefore, the hemodynamics and oxygen supply to tissues in highly resistant rats are maintained at a sufficient level for a long time.

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