Relationship between Rheological and Hemodynamic Changes in Rats with Crush Syndrome

G. A. Chernysheva, M. B. Plotnikov, V. I. Smol'yakova, A. D. Avdoshin,* A. S. Saratikov,* and T. G. Sutormina

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Narcotized rats with crush syndrome develop severe syndrome of increased blood viscosity. A strict correlation was found between changes in blood viscosity at different shear rates and total peripheral vascular resistance. The severity of central hemodynamic and hemorheological disturbances was different in rats with different reaction of total peripheral vascular resistance to injury accompanied by shock.

Key Words: *rheology; hemodynamics; crush syndrome*

Systemic hemodynamic parameters do not always adequately and fully reflect the severity of a pathological process. In 86% rats the pumping function of the heart in rats after massive blood loss remained unchanged until death [6]. Traumatic shock ran a severe course and eventuated in death in animals with a relatively high systemic blood pressure (SBP), while pronounced hypotony was associated with moderate shock [10]. This was apparently due to "functional isolation" of cardiac activity: under conditions of circulatory hypoxia cardiac output was redistributed in favor of the cardiac fraction [10].

On the other hand, microcirculatory disorders associated with increased blood viscosity, especially under conditions of generalized vasoconstriction in shock, often result in severe ischemia of organs and tissues, polyorgan failure, and poor outcome of the disease [4,6]. Therefore, analysis of blood rheology and hemodynamics are required for objective evaluation of the course of the pathological process.

The aim of this study was analysis of correlations between rheological and hemodynamic parameters in shock caused by crush syndrome (CS) in rats.

Institute of Pharmacology, Tomsk Research Center, Siberian Division of Russian Academy of Medical Sciences; *Siberian State Medical University, Tomsk

MATERIALS AND METHODS

Experiments were carried out on 33 random-bred male rats (370-400 g). In 19 animals narcotized with sodium thiopental (50 mg/kg intraperitoneally) CS was induced by 6-h compression of soft tissues of the thigh [7]. ECG was recorded 18 h after decompression in rats with CS and in intact animals under thiopental narcosis for evaluating heart rate; SBP in the femoral artery, central venous pressure in the caudal vena cava at the level of the heart, and cardiac output were evaluated by thermodilution; stroke index and total peripheral resistance (TPR) were calculated using routine formulas [10]. The volume of circulating blood was evaluated by Evans blue dilution, hematocrit, plasma and blood viscosities were evaluated using an AKR-2 rotation viscosimeter, erythrocyte aggregation by half-aggregation time ($T^1/_2$) [9], and erythrocyte deformation index was evaluated by laser difractometry [11]. Blood clotting was prevented by intravenous injection of heparin (500 U/kg). The animals were sacrificed by narcosis overdosage.

The results were statistically processed using Statistica software.

RESULTS

Eighteen hours after decompression 29% animals with CS died. These rats were classified as low resistant to

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shock due to pronounced individual sensitivity to shockogenic exposures [6]. In survivors (highly resistant rats, 71%) CS markedly increased blood viscosity, caused hypovolemia and hemoconcentration, and decreased cardiac output, stroke index, and SBP. The hemodynamic parameters changed in the same direction, but to a different degree.

Depending on changes in TPR the survivors were divided into 2 subgroups: 1) rats with clearly increasing TPR and 2) rats with decreased or unchanged TPR. N. Ya. Kovalenko *et al.* [6] observed similar changes in TPR, which presumably reflected different types of circulation and autonomic status in rats highly resistant to hemorrhagic shock.

Changes in TPR in shock are determined by two processes: bloodflow bypass of the terminal vessels and constrictive vascular reaction, as well as by neurohumoral regulation of the vascular tone. Blood viscosity also contributes to changes in TPR in deep shock: the reactive component of TRP (changes in vascular tone) decreases, while passive blood viscosity increases [10]. Analysis of correlations between TRP and blood viscosity in intact animals showed no correlation at shear rates of 300, 100, and 10 sec^{-1}. In CS, the correlation between these parameters became significant: coefficient of correlation was 0.86-0.92 at all shear rates ($p<0.005$). A similar relationship between TRP and blood viscosity at low shear rates in rats with traumatic shock was observed by S. A. Seleznev *et al.* [10].

At low shear rates, blood viscosity was largely determined by erythrocyte aggregation. A sharp drop of $T^1/_2$ in subgroups 1 and 2 (Table 1) was obviously due to hemoconcentration and blood dyscrasia due to the release of tissue degradation products during CS, which was indirectly proven by essential increase in plasma viscosity. It is well known that protein adsorption on cell membrane increases cell aggregation [13]. Adsorption of fibrinogen molecules on erythrocyte membranes stimulated their aggregation [12]. Moreover, adsorption of low- and medium-molecular-weight peptides on erythrocytes as a result of proteolytic degradation of plasma proteins (including fibrinogen), necrotic tissues, and blood cells [1,2,8] correlated with stability of erythrocyte aggregates [5]. It is noteworthy that in rats with traumatic shock electrostatic charge of erythrocytes decreases, thus facilitating erythrocyte aggregation and decreasing the suspension stability of the blood [3].

Our experiments demonstrated reduced erythrocyte deformability index in animals with CS, which clearly manifested by increased blood viscosity at high shear rates. A close inverse correlation was detected between TRP and erythrocyte deformability index (r=-0.77, p=0.05). Significant direct relationships were found between TRP and hematocrit (r=0.095, $p<0.001$) and TRP and plasma viscosity (r=0.86, $p<0.001$). The increased blood and plasma viscosities and erythrocyte deformability index in subgroup 1 (Table 1) allow us

TABLE 1. Rheological and Hemodynamic Parameters of Rats with CS ($M\pm m$)

Parameter	Intact animals	CS	
		subgroup 1	subgroup 2
TRP, dyn×sec×cm^{-5}	2.85±0.12	4.55±0.47*	2.42±0.14*#
Cardiac output, ml/min/kg	339.4±16.4	186.6±22.9*	256.5±23.0*+
Stroke index, ml/kg	0.84±0.04	0.47±0.05*	0.66±0.04*+
Heart rate, str/min	412±9	378±12	392±21
SBP, mm Hg	123±3	98±3*	75±6*+
Central venous pressure, mm H_2O	15±2	9±1*	14±2+
Volume of circulating blood, ml/kg	61.33±2.24	38.46±2.24*	52.02±3.52*+
Blood viscosity, cP, at shear rate 1 sec: 300	4.1±0.1	6.8±0.7*	5.1±0.3*+
100	4.8±0.1	9.0±1.3*	5.9±0.3*+
10	9.5±0.3	16.3±1.1*	12.7±1.0*+
Plasma viscosity, cP,	1.5±0.03	2.2±0.2*	1.7±0.03*+
Hematocrit, %	46±1.2	54±1.8*	49±1.1
$T^1/_2$, sec	10.3±1.3	2.0±0.1*	2.2±0.05*
Erythrocyte deformability index at 360/sec, rel. units	0.244±0.009	0.175±0.002*	0.208±0.006*+

Note. $p<0.05$: *vs.* intact rats, +*vs.* subgroup 1.

to conclude that different reactions of TPR to shock depend on the severity of the increased blood viscosity syndrome.

Analysis of hemodynamic parameters in each subgroups separately essentially reduced data scattering and revealed differences between the subgroups. The rats with moderately decreased TRP (15% in comparison with intact animals) had higher circulating blood volume, central venous pressure, cardiac output, and stroke index and lower SBP than animals with increased TRP (Table 1). In rats with TRP increasing in response to shock, the compensatory mechanisms maintaining relatively high SBP aggravated disturbances in transcapillary mass exchange with rapid loss of the liquid fraction of the blood, hemoconcentration, development of more pronounced syndrome of increased blood viscosity, essential decrease in the circulating blood volume with a decrease of venous return to the heart, and decreased stroke index and cardiac output. In animals with moderately decreased TRP, the vascular tone decreased, which maintained more adequate blood supply to organs and tissues even under conditions of decreased perfusion pressure and increased blood viscosity.

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