DISTURBANCES OF BLOOD RHEOLOGY AFTER RESUSCITATION FROM AN AGONAL STATE

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Early normalization of disturbances of the microcirculation and rheologic properties of the blood in shock and blood loss can prevent the development of severe, often irreversible hypoxic disturbances in the CNS and internal organs [2, 4-9, 11].

In the investigation described below the time course of some rheologic characteristics of the blood was studied during agony arising through prolonged and massive blood loss and after resuscitation. At different times of the postresuscitation period the effect of hemodilution by repeated infusions of dextran on the state of flowability of the blood was studied.

EXPERIMENTAL METHODS

Experiments were carried out on 12 heparinized (500 I.U./kg) dogs of both sexes weighing 10-12 kg. Under superficial pentobarbital anesthesia with trimeperidine premedication (8 mg/1 kg body weight) the animals were exsanguinated quickly (in 5-7 min) from the femoral artery until the blood pressure (BP) had fallen on average to 40 mm Hg, at which level it was maintained for 2 h. By further blood loss BP was then lowered until the terminal pause (brief respiratory arrest) ensued. The duration of the terminal state varied in the experiments from 2 h 4 min to 2 h 12 min. The total blood loss was 50 ± 4 ml/kg. Revival of the animals began in the agonal period. The lungs were artificially ventilated with 100% oxygen with a respiratory volume of 40 ml/kg and respiration rate of 16-20 cycles/min. Reperfusion was performed through the femoral artery. Artificial ventilation of the lungs was stopped when the lost blood had been made good. After reperfusion of the blood, dextran was injected by intravenous drip (20-25 ml/kg) under control of the central venous and arterial pressure and ECG, recorded on a polygraph (San-Ei, Jaoan). Infusion of dextran (10 ml/kg) with heparin (500 I.U./kg) was repeated after 24 h. All the animals survived. Samples of blood for determination of viscosity, flowability limit, and hematocrit index were taken from the femoral artery at the following stages of the experiment: in the initial state, during the period of agony, after reinfusion of blood, 60 min after infusion of dextran, and also on the 1st day (before infusion of dextran), the 5th-7th day, and after 1-3 months of the post-resuscitation period. To determine the viscosity of the blood a rotary viscosimeter (VIR-75), made at the Gor'kii Physicotechnical Institute, was used. The blood viscosity was determined in mPa-sec with a shear stress of 2 to 200 dynes/cm^2, corresponding to a shear velocity of 1.3 to 52.4 sec^{-1}. The flowability limit of the blood was calculated by Casson's graphic method [10].

EXPERIMENTAL RESULTS

During the agonal period because of spontaneous hemodilution (the hematocrit index fell by 0.08 liter/liter) there was a significant fall in blood viscosity at low shear velocities: by 4.8 mPa-sec at 1.34 sec^{-1}, by 4.55 mPa-sec at 8.38 sec^{-1} (Table 1). A similar trend of changes in rheologic properties of the blood was found in hemorrhagic shock in the decompensation stage [3].

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TABLE 1. Changes in Rheologic Properties of Blood in Animals Resuscitated from an Agonal State (M ± m)

Stage of experiment	Viscosity of blood (in mPa-sec) with shear velocity of					Hematocrit	Flowability limit, dynes/cm^2
	1,34sec^{-1}	3,35sec^{-1}	8,38sec^{-1}	20,9sec^{-1}	54,2sec^{-1}		
Initial state (n= 12)	13,4±1,6	10,9±1,6	7,2±0,5	5,6±0,8	4,5±0,2	0,47±0,02	0,18±0,01
Agony (n= 7)	8,6±0,7*	6,35±0,9*	5,1±0,2*	4,2±0,2	4,2±0,3	0,39±0,01*	0,15±0,02
After intra-arterial infusion of blood (n= 11)	18,2±0,9*	13,6±0,6	9,0±0,5*	6,5±0,3	5,2±0,2	0,51±0,02	0,34±0,02*
60 min after intravenous infusion of dextran (n= 12)	10,8±1,4	8,7±0,8	6,5±0,5	5,35±0,1	4,3±0,1	0,37±0,05*	0,21±0,02
After resuscitation:							
1st day (before dextran infusion) (n= 11)	11,8±0,4	9,8±0,7	6,3±0,5	5,6±0,3	4,3±0,1	0,37±0,00*	0,22±0,04
5th-7th day (n= 7)	10,9±1,5	7,8±1,0	5,9±0,8	4,8±0,1	3,1±0,2*	0,26±0,02*	0,18±0,003
1-3 months (n= 3)	20,2±0,8*	14,08±1,3	9,2±1,1	6,7±1,1	5,3±0,1*	0,55±0,02*	0,41±0,02*

Legend. *P < 0.05 compared with initial values; n) number of observations.

After reinfusion of the blood its viscosity was substantially increased. For instance, the viscosity of the blood rose by 4.8 mPa-sec compared with its value before the experiment, with a shear velocity of 1.34 sec^{-1}. Meanwhile a tendency was observed for viscosity to rise at other shear velocities also (8.38 and 54.2 sec^{-1}). The flowability limit of the blood was almost doubled compared with the initial state. Changes in the hematocrit index after replacement of the lost blood were very small (Table 1). The early post-resuscitation period after agony is thus characterized by profound disturbances of the rheologic properties of the blood, and consequently, by substantial disturbances of the microcirculatory system.

Infusions of dextran (20-25 ml/kg) were started immediately after replacement of the lost blood, and they significantly lowered the hematocrit index (by 0.1 liter/liter). The viscosity and flowability limit of the blood were restored to normal at all shear velocities tested. During the first day the parameters of the flow properties of the blood, under conditions of moderate hemodilution (hematocrit 0.37 liter/liter) were indistinguishable from those observed initially (Table 1).

A high concentration of dextran in the blood, especially after repeated (on the 1st day) injection of the plasma expander, led to further hemodilution. For instance, on the 5th-7th day the hematocrit fell by 0.13 liter/liter (P < 0.05) compared with the previous stage (Table 1). The flowability limit of the blood remained at its initial values during the first week of observation. Meanwhile the viscosity of the blood at high shear velocities (54.2 sec^{-1}) was significantly reduced by 1.4 mPa-sec. At all other shear velocities tested these parameters did not differ significantly from their initial values. It follows from these results that preservation of the initial level of the blood flowability limit with the development of profound hemodilution (0.26 liter/liter) reflects considerable changes in the rheologic properties of the blood during the first week after resuscitation.

Between 1 and 3 months after resuscitation there was a significant increase in viscosity of the blood by 6.8 and 0.8 mPa-sec respectively at low (1.34 sec^{-1}) and high (54.2 sec^{-1}) shear velocities respectively compared with the initial data. The flowability limit of the blood was more than doubled. The hemoconcentration also increased (by 0.08 liter/liter; P < 0.05), evidence of a prolonged disturbance of vascular permeability in the postresuscitation period. In these states, the permeability of the cell membranes increases sharply [1]. However, the degree of increase in the blood flowability limit was much greater than the rise in the hematocrit index. This is indirect evidence of impairment of the actual rheologic properties of the erythrocytes.

The persistent increase in blood viscosity was thus due not only to severe hypoxic impairment of cellular and vascular permeability, which lasted 1-3 months after resuscitation, but also to a disturbance of other rheologic mechanisms in agonal states. Consequently, hemodilution by dextran in the postresuscitation period did not abolish the disturbances of blood flowability for a long time after resuscitation. This long persistence of disturbed blood flowability may be one of the mechanisms of formation of delayed postresuscitation pathology of the CNS and parenchymatous organs observed in both clinical and experimental

practice [4, 5]. It can be tentatively suggested that the timely correction of the disturbed rheologic properties of the blood after revival from the agonal state by properly oriented pathogenetic treatment is an important component in the prophylaxis of postresuscitation complications.

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ROLE OF ARACHIDONIC ACID IN PLATELET AGGREGATION INDUCED BY *Salmonella typhimurium* ENDOTOXIN

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Much evidence has recently been obtained to show that many functions of platelets are under the controlling influence of arachidonic acid (AA) and its metabolic products — the prostaglandins (PG). Meanwhile many aspects of the mechanism of their action are still unexplained. In particular, the role of PG in changes in platelet function under the influence of endotoxins of the agents of many infectious diseases has not been adequately studied. Yet endotoxinemia in infectious diseases (acute intestinal infections, meningococcal infections, septic states) is an essential factor determining disturbance in the hemostasis system and leading to thrombo-hemorrhagic complications which aggrevate the course of these diseases [3-6].

Endotoxins of Gram-negative bacteria (*Salmonella typhimurium, Neisseria meningitidis*) have been shown to induce aggregation of platelets from normal bood donors. Meanwhile scanning microscopy has revealed morphological changes in platelets reflecting their activation by endotoxins. In this connection data showing that during activation of platelets there is a sharp increase in PG biosynthesis from AA, which is a component of the phospholipids of their membranes, are of considerable interest [9]. These observations indicate that PG play an essential role also in platelet aggregation induced by endotoxin.

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