CIRCULATING PLASMA PROTEINS IN EXPERIMENTAL ACUTE BLOOD LOSS AND AFTER TRANSFUSION OF BLOOD COMPONENTS

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Pathogenetic combination therapy of acute blood loss must include in every case replacement of the lost fluid, restoration of oxygen transport and the electrolyte balance, and maintenance of the colloid-osmotic pressure and other parameters of the blood [5]. The efficacy of treatment largely depends on the degree of the plasma protein deficiency and of the various disturbances of homeostasis connected with it [4, 7, 8]. Among the list of factors influencing the magnitude of the protein deficiency may be included the volume and rate of the blood loss, the duration of hypotension, and the character of the treatment given [2, 3].

The aim of the investigation was an experimental study of reactive changes in proteins in the circulation after acute lethal blood loss and combination treatment with infusion and transfusion.

EXPERIMENTAL METHOD

Experiments were carried out on 35 mongrel dogs, male and female, weighing from 7 to 20 kg. The animals were anesthetized with pentobarbital (30 mg/kg). The blood pressure (BP) was recorded in the arch of the aorta by means of a "Biomedica" cardiomonitor (Italy). The circulating blood volume (CBV) was determined by the label dilution method, using human serum albumin labeled with ^{131}I (commercial preparation) or the dyes T-1824 and Cardiogreen. Radioactivity was measured on a "Gamma" apparatus (Hungary) and the quantity of dye by the Cardiac Output Computer (USA). To calculate the circulating plasma volume (CPV) the dilution data, CBV, and hematocrit index were used. A model of acute blood loss [1] with blood withdrawn from the femoral artery until BP could no longer be determined, was used. The volume of blood removed (VBR) varied in different individuals from 45 to 85% of CBV, measured before blood loss (average 55.0 ± 2.4 ml/kg). Infusion of salt solutions (I1), namely lactasol and polysol (quintasol) [1] or of a mixture of polysol with polyglusol (80:20) began 2 min after respiratory arrest. Transfusion of blood components (I2) began 2 h after the end of I1. The source of the components for I2 was the recipient dog's own blood, removed from the femoral artery (the autologous version) or blood from a donor dog, kept at 4°C for 14-16 h (allogeneic version). Blood prepared in a solution of the Soviet plasma expander glugitsir was centrifuged at 2000 rpm for 10 min. The erythrocytes were washed with physiological saline three times, and immediately before infusion they were diluted until the hematocrit value was 0.40-0.50 liter/liter. The plasma was mixed with the glugitsir solution in the ratio of 1:0.5 to 1:0.7. All preparations were injected into the femoral vein: the crystalloids at the rate of 30-60 ml/min in a volume of 1.5 of VBR, the erythrocytes at the rate of 15-20 ml/min and in a volume of 0.5-0.7 of VBR, plasma at the rate of 10-20 ml/min in a volume of 0.3-0.6 of VBR. The control animals were given infusion therapy with protein-free plasma ultrafiltrate or a mixture of lactasol plus polyglusin in a volume of one to three VBR and at the rate of 30-50 ml/min. Depending on the composition of I2 the experimental animals were divided into four groups: 1) autologous erythrocytes (auto-E), 2) allogeneic erythrocytes (allo-E), 3) autologous plasma (auto-P), and 4) allogeneic plasma (allo-P). Blood samples were taken in the initial state (anesthesia), at the time of ending of blood withdrawal, 10 min and 2 h after the end of I1, and 10 min and 2 h after the end of

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TABLE 1. Circulating Plasma Volume (ml/kg) and Protein Concentration (g/liter) during Posthemorrhagic Infusion of Salt Solutions (I1) and Blood Components (I2; M ± m)

Group	Parameter	Original state	I1		I2	
			10 min	2 h	10 min	2 h
Control	CPV	42,4±3,1	57,9±6,0	42,5±3,1	—	40,6±4,6***
(7)	C	57,7±2,0	18,8±1,7	23,4±3,0	—	25,8±2,9***
First auto-E	CPV	55,5±5,0	93,5±7,5	59,6±6,4	62,0±5,1	54,5±7,4
(8)		P0	P0	P0		P0
	C	59,8±2,0	17,6±1,4	23,9±0,9	19,3±2,0	26,0±1,4
Second allo-E	CPV	47,7±2,9	80,1±11,4	52,4±6,8	59,7±6,4	48,9±5,5
(5)			P0			
	C	58,8±3,6	21,0±2,3	30,3±3,1	27,0±3,1	34,4±3,4
			P0, P1	P0, P1	P1	P0, P1
Third auto-P	CPV	45,2±4,8	65,6±12,9	50,4±7,4	71,4±9,4	64,4±11,2
(7)						
	C	58,6±2,6	24,0±1,2	31,3±1,7	34,7±2,3*	40,5±2,9*
			P0, P1	P0, P1	P1, P2	P0, P1, P2
Fourth allo-P	CPV	43,1±1,8	63,0±7,8	43,5±3,8	81,2±11,1	63,1±4,7
(8)		P1	P1	P1		P0, P2
	C	62,7±3,0	25,4±2,5	33,2±2,9	39,4±3,2**	45,4±3,7**
			P0, P1, P2	P0, P1	P1, P2	P0, P1, P2, P3

Legend. *) Six dogs, **) five dogs, ***) 4 h after I1. Only significant differences ($p \leq 0.05$) are indicated; PO) compared with control, P1) with Group 1, P2) with Group 2, P3) with Group 3. Number of experiments given in parentheses.

The trend of the changes in the parameters during component therapy (I2) differed from that described after I1. I2. In dogs of the control group (without I2) samples were obtained 10 min and 2 and 4 h after I1. The total protein concentration (C) in the plasma was determined spectrophotometrically and verified by Lowry's method [2]. The circulating protein was calculated by the equation P (in g/kg) = C × CBV. The results were subjected to statistical analysis by parametric tests [6].

EXPERIMENTAL RESULTS

Values of CPV and the blood protein levels in the initial state were characterized by satisfactory stability (Table 1). After blood loss and injection of salt solutions, short-term hypervolemia (10 min) developed, varying in degree greatly in different individuals, and accompanied by a relatively less marked but more prolonged hypoproteinemia. The value of CPV returned to its initial level 2 h after the end of I1, but the plasma protein concentration remained low for 4 h or more after I1. The composition of I1 had no significant effect on changes in the values of CPV or the blood protein level (Fig. 1). The protein concentration 10 min after infusion of polysol was 32% of the initial value, rising to 44% 2 h later; after infusion of lactasol the corresponding values were 37 and 47%, and after infusion of the plasma ultrafiltrate, 33 and 42%. The value of CPV measured after 10 min was 78.6% of the calculated value (CPV_{orig} — VPR + I1) and continued to decrease after 2 h, when it was 56.4%. This can be explained by the rapid redistribution of fluid moving from the blood stream into the extravascular space. The rate of increase of the circulating protein concentration did not depend on the level of proteinemia at the time of ending of I1 and it varied in animals of the different groups from 3.2 to 4.6 g/liter·h.

CPV did not change significantly after transfusion of erythrocytes, but conversely, it rose abruptly and significantly after injection of plasma. This difference was expressed both relative to the original value of CFV (Table 1) and when the measurements of CPV were compared with its calculated values (CPV 2 h after I1 plus the volume of I2). CPV 10 min after transfusion of erythrocytes averaged 62-66% of the calculated value, but after transfusion of plasma it was 94-113%. In Groups 3 and 4 the hypervolemia lasted not less than 2 h, and was due to the water-retaining action of the injected protein. In the case of transfusion of erythrocytes there was a short additional decrease in the level of the proteinemia as a result of dilution of the plasma with the salt solution used to resuspend the cells. After plasma transfusion the protein concentration rose moderately on account of exogenous protein, but did not reach its original level within 2 h. The relative increase in the level of proteinemia was somewhat less in the allo-P group than in the auto-P group.

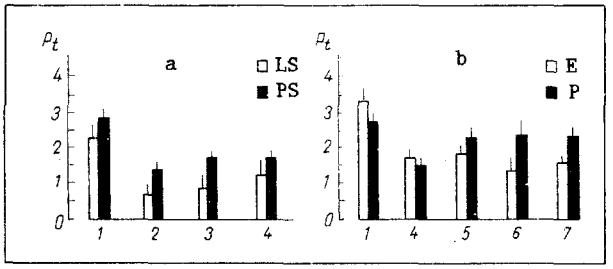

Fig. 1. Protein concentration (g/kg) in circulating plasma of dogs during post-hemorrhagic infusion of salt solutions (a) and blood components (b). 1) Initial state, 2) after blood loss, 3) 10 min after end of It, 4) the same 2 h later, 5) immediately after the end of I2, 6) 10 min after I2, 7) 2 h after I2; a: unshaded columns — lactosol (LS), black columns — polysol (PS); b: unshaded columns — erythrocytes (E), black columns — plasma (P).

Thus in the acute period after blood loss and after treatment by infusion and transfusion, the control of protein-volemic equilibrium was profoundly disturbed. Successive injections of salt solutions and blood components were accompanied by the development of hypervolemia and hypoproteinemia, the potential danger from which was the greater, the more dilute the plasma, and the smaller the amount of exogenous protein injected. Massive infusion of protein-free solutions potentiates the effect of natural autohemodilution, creating an additional volemic load on the vascular system. Under these conditions a certain part of the proteins leaves the blood stream actually during infusion, and within a short time after its end. Under the influence of blood component therapy these disturbances are only partly compensated, depending on the degree of correction of the hypoproteinemia. Transfusion of erythrocytes improves the oxygen transporting function of the blood, but under these circumstances the hypoproteinemia becomes aggravated and this may lead to the development of irreversible disorders. Transfusion of plasma in a volume of 0.5 of VBR leads to an increase in the protein concentration up to 60-70% of the initial level, which is evidently sufficient to maintain the protein-dependent functions of the blood (colloid-osmotic, rheologic, transport, buffer, detoxicating) for several hours, until the reserve proteins are mobilized and protein synthesis de novo is stimulated. However, the quantity of protein in circulation remains below the normal level, preventing the effective attainment of normovolemia. The interdependence of protein-volemic relations in the blood system requires modification of the treatment program in order to reduce to a minimum the inappropriate changes in CFV and in the circulating protein concentration during posthemorrhagic infusion of the solutions and blood components. The function of the whole system must be to optimize the quantity of circulating protein and its composition, thereby maintaining the water-retaining properties of the proteins and the related normovolemia.

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