WATER-BINDING COMPONENTS OF BLOOD PLASMA DURING ENTERAL CORRECTION OF POSTHEMORRHAGIC HYPOVOLEMIA

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UDC 616.151.11-02:616-005.1]-085.384-032:611.34]-092.9

KEY WORDS: enteral correction; hypovolemia; water-retaining components of plasma

In addition to the infusion—transfusion method of treatment of posthemorrhagic hypovolemia, in recent years the method of its enteral correction has been used [5, 8]. The method is based on injection into the intestine of an electrolyte-monomer solution, whose constituents correspond in concentration to those observed in the chyme of healthy animals, and which promote its rapid absorption [5, 9].

The efficacy of this method of treatment, like that of other methods of infusion therapy of blood loss, depends on stability of replenishment of the plasma deficiency. In turn, stable replenishment of the lost plasma takes place through restoration of the volume of water-retaining components of the plasma, structurally connected into an organized water—protein—electrolytes system [1, 4, 12, 13]. We could find no research published in the accessible literature, devoted to the study of the role of the digestive apparatus in the formation of the water-retaining system of the plasma and the effect of enteral correction of blood loss of varied severity on the parameters of the blood volume. The investigation described below was to study these problems.

EXPERIMENTAL METHOD

Experiments were carried out on dogs with a chronically implanted fistula into the duodenum. At the beginning of the experiments, under general anesthesia (per 10 kg body weight — Callipsol 2, relanium 2, trimeperidine 2) a transducer for impedanceometry was inserted through the femoral vessels into the aorta, and catheters also were inserted into the aorta and inferior vena cava. Various degrees of bleeding (20, 30, and 40 ml/kg body weight) were carried out in one stage at the rate of 0.7 ml/kg·min. The electrolyte-monomer solution [9] was injected through the fistula into the duodenum 30 min after the end of blood loss, the rate of injection being controlled by the motor evacuatory function of the intestine, and amounted on average to 10 ml/min. A blood loss of 50 ml/kg was carried out in two stages with an interval of 60 min after the loss of 20 ml/kg of blood. Enteral correction began during repeated bleeding. The volume of solution injected was 1.5 times greater than the volume of blood lost. In successive stages of the experiment the following parameters were determined: circulating blood volume (CBV) by the impedance method [10], hematocrit (Ht), concentration of total serum proteins and albumins (by the biuret method), sodium and potassium (by flame photometry), and the osmotic and oncotic pressure (by instruments from "Knauer"). The plasma and cell volumes of the blood (PV and CV), the total circulating protein (TCP), albumin (TCA), sodium ($TCNa^+$), and potassium (TCK^+) concentrations were calculated. The results obtained during the experiments were subjected to statistical analysis. Altogether 42 experiments were conducted on 38 dogs.

EXPERIMENTAL RESULTS

The experimental data after analysis are given in Tables 1 and 2. It will be clear from these tables that blood loss led to changes in the volume characteristics, the severity of which increased with an increase in the volume lost. It was discovered that, despite an increase in plasma volume as a result of physiological hemodilution [14, 15], with an increase in the volume of blood lost the CBV deficiency increased, and reached an average value of 43% for blood loss of 40 ml/kg and 57% for blood loss of 50 ml/kg.

Laboratory of Experimental Pathology, N. V. Sklifosovskii Emergency Aid Research Institute, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. K. Permyakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 110, No. 12, pp. 580-582, December, 1990. Original article submitted March 1, 1990.

0007-4888/90/0012-0025$12.50

TABLE 1. Changes in CBV, Its Components, and Parameters of Blood Proteins after Blood Loss of Varied Severity and after Its Enteral Correction

Procedure	CBV	CVP, ml/kg	CV	Total serum proteins		Albumins	
				g/liter	g/kg	g/liter	g/kg
Initial data ($n=42$)	79,1±2,0	43,5±1,6	36,2±1,6	56,4±1,01	2,45±0,13	25,1±0,8	1,08±0,07
15-30 min after blood loss in a volume of:							
20 ml/kg ($n=25$)	65,0±2,0*	38,1±1,0*	26,8±1,6*	44,3±0,89*	1,68±0,06*	18,0±0,06*	0,67±0,05*
30 ml/kg ($n=11$)	56,4±1,5*	32,8±0,71*	23,5±2,0*	42,2±0,78*	1,38±0,06*	—	—
40 ml/kg ($n=11$)	45,1±1,3*	25,9±0,39*	19,1±2,1*	42,4±0,71*	1,06±0,04*	—	—
50 ml/kg ($n=7$)	34,2±0,63*	18,8±0,18*	15,3±1,9*	48,7±0,98*	0,91±0,06*	21,2±0,9*	0,40±0,03
After correction of blood loss with a volume of:							
20 ml/kg ($n=25$)	80,0±2,4**	53,6±1,8**	27,1±2,9	41,5±0,75	2,20±0,17	17,6±0,6**	0,93±0,08
30 ml/kg ($n=11$)	70,6±1,9**	48,7±1,4**	22,2±2,8	32,5±0,68**	1,56±0,06	—	—
40 ml/kg ($n=11$)	65,0±1**	47,2±1,6**	18,0±2,0	31,5±0,66**	1,48±0,06**	—	—
50 ml/kg ($n=13$)	58,0±1,1**	44,7±1,2**	13,3±1,9	36,0±0,67**	1,61±0,06**	1,53±0,5**	0,68±0,06**

Legend. Here and in Table 2: *) significance of differences compared with initial data, **) significance of differences compared with data obtained after loss of corresponding volume of blood.

TABLE 2. Changes in Electrolyte Concentration and Osmotic and Oncotic Pressure after Blood Loss of Varied Severity and Its Enternal Correction

Procedure	Plasma sodium		Plasma potassium		Osmotic pressure, milliosmoles/liter	Oncotic pressure, mm Hg
	mmoles/liter	mmoles/kg	mmoles/liter	mmoles/kg		
Initial data ($n=42$)	144,2±1,74	6,26±0,35	3,88±0,09	0,16±0,02	284±6,3	23,4±0,51
After blood loss with a vol. of:						
20 ml/kg ($n=25$)	145,3±2,32	5,48±0,29	3,72±0,08	0,14±0,02	276±8,6	—
30 ml/kg ($n=11$)	150,0±2,47	4,90±0,27*	—	—	277±7,8	20,2±0,37
40 ml/kg ($n=11$)	152,1±2,04	3,80±0,23*	—	—	280±8,3	18,9±0,35*
50 ml/kg ($n=7$)	155,4±2,12*	2,93±0,18*	4,70±0,15*	0,09±0,01*	314±8,3*	—
After correction of blood loss with a vol. of:						
20 ml/kg ($n=25$)	145,0±1,98	7,55±0,45**	3,60±0,07	0,19±0,02	270±8,1	—
30 ml/kg ($n=11$)	143,4±2,18	6,88±0,40**	—	—	275±8,3	22,5±0,63
40 ml/kg ($n=11$)	150,0±2,44	7,04±0,43**	—	—	273±8,0	19,7±0,39
50 ml/kg ($n=13$)	141,5±2,48**	6,30±0,37**	3,66±0,06**	0,16±0,03**	285±8,1	

The biochemical investigations showed that irrespective of the severity of blood loss, the plasma sodium concentration remained stable and the potassium concentration rose. However, because of the posthemorrhagic reduction of the plasma volume, the masses of sodium and potassium were reduced proportionally. Investigations of protein and albumin concentrations in the blood serum showed that their decrease during blood loss of up to 40 ml/kg was greater than after blood loss of 50 ml/kg. The decrease in the protein concentration combined with reduction of PV led to an increasing reduction of their mass, which reached maximal values after blood loss of 50 ml/kg. Osmometry revealed high stability of the plasma osmotic pressure after blood loss of not more than 40 ml/kg. A tendency for it to rise was recorded only after blood loss of 50 ml/kg. At the same time the oncotic pressure fell with an increase in volume of blood loss, reflecting the dynamics of CVP. Analysis of data obtained during experiments with blood loss showed that only after bleeding to the extent of 50 ml/kg (60-70% of CBV) did critical reduction of the protein and electrolyte mass cause a sharp disturbance of the water-retaining structure of the plasma.

Increasing hypovolemia coupled with hyperosmolarity of the plasma and hemodynamic disorders [5, 9] heralded irreversible changes, which developed after blood loss of 50 ml/kg [1, 4, 6, 7]. As our previous investigations showed, during blood loss of this volume the absorptive function of the small intestine was inhibited [5]. Intestinal infusion of solution after blood loss of 50 ml/kg was therefore started actually during bleeding. Enteral correction of blood loss of smaller volumes began 30 min after the end of bleeding.

The aim of the next group of experiments was to study the effect of absorption of the electrolyte-monomer solution on parameters of the water-binding components of the plasma and on the efficacy of enteral correction of posthemorrhagic hypovolemia. Analysis of the data obtained in the course of these experiments (Tables 1 and 2) showed that as a result of absorption of the solution a positive trend of the changes in the volemic parameters was observed, to a degree which depended

on the volume of blood loss and on the original parameters. Ht decreased, PV increased, and so also did CBV. The concentration of protein and albumin fell even more, but with an increase in plasma volume, their volume parameters increased, as also did the plasma oncotic pressure. The investigations showed that after enteral correction all animals subjected to blood loss of 20, 30, and 50 ml/kg survived. Enteral infusion of solution, given 30 min after blood loss of 40 ml/kg, did not prevent a lethal outcome in 15% of cases. In a study of the mechanisms leading to stable replenishment of PV and maintenance of the animals' life, it was found that irrespective of the reduction in the mass of sodium after blood loss, $CVNa^+$ not only rose to the original values, but actually exceeded them. The dynamics of changes in CVP and CVA, the mass of which doubled after correction of blood loss of 50 ml/kg, was similar but less marked (Table 1). However, if the increase in the plasma sodium concentration could have been due to its transport into the blood as a result of absorption from solution and compensatory resorption in the kidneys [4, 7, 9], the increase in CVP was due entirely to the intake of endogenous proteins, Synthesis of plasma proteins in the liver is known to take place slowly [11], and the passage of interstitial proteins along the lymphatics into the blood stream likewise cannot replace their deficiency quickly [15]. Consequently, other mechanisms of plasma protein formation must exist.

Experimental studies have shown that ^{14}C-glycine and ^{35}S-methionine, injected into an isolated segment of small intestine in the composition of amino acids, are incorporated into the plasma proteins of blood and lymph draining from this segment of intestine, evidence of their synthesis in the intestinal wall [2, 3]. There is every reason to suppose that the increase in CVP observed in the present experiments after enteral correction of blood loss also was due to protein synthesis in the wall of the small intestine, from amino acids supplied in the composition of the enteral solution, and also from endogenous amino acids. Another possibility is that the glucose, a component of this solution, is involved in the supply of energy for protein synthesis. Support for this view is given by the fact, which we established previously, that the rate of assimilation of amino acids and glucose by the mucous membrane of the small intestine during infusion of the collecting solution is increased in the posthemorrhagic period [9].

Thus the rapid and stable increase in the CBV, CUP, $CVNa^+$, and CVK^+, discovered in these experiments, is evidence in support of the involvement of the digestive organs in restoration of the water-retaining components of the plasma.

Stable replenishment of the plasma deficiency after enteral correction of acutely developing hypovolemia is evidently determined by the fact that it is during absorption of water and electrolytes that endogenous plasma proteins, including those synthesized by the intestinal wall, enter the blood stream, and that the conditions are right for the formation of a structurally bound water—protein—electrolytes system. These mechanisms, taken as a whole, may determine the rapid restoration of the plasma volume and maintenance of volemic homeostasis after correction of posthemorrhagic plasma loss by injection of an electrolyte-monomer solution into the intestine.

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