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POSTRESUSCITATION TOXEMIA AND ITS POSSIBLE CORRECTION BY ALBOSORB

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Endogenous toxemia arising in terminal and postresuscitation states significant complicates the course of postresuscitation sickness [7]. A promising trend in detoxication is the use of additional transport agents, binding toxins and conveying them to their points of excretion, degradation, or adsorption [3, 9].

The aim of this investigation was to study the efficacy of albosorb, a product obtained from albumin treated on charcoal adsorbents, and possessing increased adsorptive capacity for ligands of different nature, in the postresuscitation period [5, 6].

EXPERIMENTAL METHOD

Experiments were carried out on 40 dogs weighing 12-25 kg, anesthetized with pantopon (8 mg/kg) and pentobarbital (5-10 mg/kg). The animals were subjected to clinical death from exsanguination, for a period of 10 min. Resuscitation was carried out by intraarterial injection of blood with adrenalin and artificial ventilation of the lungs with 80% oxygen. In the 15 experiments of group 1, 5-7 min after restoration of cardiac activity, and at a time of incomplete restoration of the blood loss (by 10-20 ml/kg), albosorb was injected in a dose of 7-10 ml/kg over a period of 25-30 min. In the eight experiments of group 2, a pharmacopoieal preparation of albumin was injected in the same volumes. The animals of group 3 (17 experiments) received no additional treatment. Before blood loss and between 15 min and 6 h after resuscitation, biochemical and physiological tests were carried out. The total content of molecules of average molecular weight (MAMW) [1] was determined in the blood plasma. Concentrations of components with mol. wt. of up to 30,000 daltons in the ultrafiltrate of plasma obtained with the aid of PT-30 membrane filters (Amicon, USA), were determined by high-pressure liquid chromatography (HPLC system from LKB, Sweden). The binding capacity of the plasma proteins relative to weakly bound ligands was estimate by the use of the total area of chromatographic peaks corresponding to the above-mentioned components [6]. The ability of plasma proteins to form complexes by hydrophobic interaction was assessed relative to Congo Red [8]. The osmotic resistance of the erythrocytes to hypotonic hemolysis was determined by the method in [4] and the colloid osmotic pressure (COP) by means of a colloid osmometer from Knauer (West Germany). The cardiac output was measured by the thermodilution method, and the systolic and pulmonary arterial pressures and heart rate were recorded. Oxygen saturation, partial pressure, and concentration, hemoglobin concentration, and hematocrit were determined in arterial and mixed venous blood, and the total oxygen consumption was calculated.

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TABLE 1. Changes in Binding Capacity of Plasma, Concentration of Molecules of Average Molecular Weight, and Some Parameters of the State of the Blood and Hemodynamics and of Metabolism in Dogs after Resuscitation (M ± m)

Parameter	Experimental group	Postresuscitation period		
		initially	15–30 min	3–6 min
Concentration of MAMW, conventional units	1	0,231±0,013	0,217±0,011	0,205±0,009
	2	0,214±0,015	0,259±0,01*	0,220±0,010
	3	0,247±0,016	0,310±0,015*	0,252±0,009
Binding capacity of plasma for hydrophobic ligands, mg dye/mg protein	1	0,091±0,012	0,137±0,016*	0,124±0,018*
	2	0,084±0,012	0,094±0,013	0,110±0,017
	3	0,083±0,010	0,041±0,015*	0,036±0,010*
Binding capacity of plasma for hydrophilic ligands, total area of peaks with mol. wt. of 20,000 × 10^4	1	114±20	119±22	102±20
	2	147±18	211±64*	154±27
	3	148±17	208±16*	171±25*
COP, mm Hg	1	19,1±0,13	17,5±0,38	19,6±0,46
	2	18,9±0,15	17,7±0,41	19,0±0,39
	3	19,0±0,15	16,2±0,38	17,3±0,51
Degree of hemolysis of erythrocytes, %	1	10,81±1,22	21,81±3,60*	15,21±3,60
	2	10,80±1,27	28,76±4,27*	23,48±4,03*
	3	9,26±0,91	31,14±1,30*	32,10±3,09*
Cardiac index, ml/kg·min	1	130,8±8,6	134,4±7,0**	116,0±9,6**
	3	129,4±7,5	106,5±12,1	78,3±6,1
Oxygen consumption of the body, ml/kg·min	1	7,02±0,52	6,24±0,43**	8,95±1,15
	3	6,30±0,47	4,22±0,35	7,19±0,58
Hematocrit, liter/liter	1	52±2	47±1	47±1**
	3	51±2	50±2	54±1
T °C of blood in aorta	1	36,4±0,3	34,7±0,2	36,7±0,3**
	3	36,4±0,3	35,1±0,3	35,4±0,3

Legend. *$p < 0.05$ compared with initially, **$p < 0.05$ compared with group 3.

EXPERIMENTAL RESULTS

The investigations showed that 5 min after resuscitation large quantities of toxic products had entered the blood stream from the tissues: the MAMW level had increased to 173% of the initial value. By the 30th minute after resuscitation, the work of the intrinsic detoxicating systems of the body had led to a decrease of MAMW to 125% of the initial value (group 3), and to 120% in the experiments with pharmacopoieal albumin (group 2), followed by a fall to the original level after 3 h. Injection of albosorb, however, led to binding of toxic ligands, and the whole postresuscitation period, under our observation, was characterized by lower than original concentrations of MAMW (94% 30 min and 89% 3 h after resuscitation) (Table 1).

The study of the binding capacity of blood plasma for toxic substances of hydrophobic nature showed that in the experiments of control group 3 this capacity was considerably depressed throughout the postresuscitation period (49-43% of the initial value). Injection of pharmacopoieal albumin considerably increased the binding capacity of the plasma (to 111% 30 min, and to 130% 3 h after resuscitation). The most favorable results were obtained by injection of albosorb, which increased the binding capacity of the plasma for hydrophobic ligands to 145% of the initial value 30 min after resuscitation (Table 1).

After injection of albosorb virtually all toxic hydrophilic ligands were bound The total area of the peaks of these substances with molecular weight of under 20,000 daltons did not exceed the initial level at any time of observation. After injection of pharmacopoieal albumin and in the experiments of the control group, the early postresuscitation period was characterized by a large excess of hydrophilic molecules in the blood.

The use of albosorb and pharmacopoieal albumin led to normalization of COP of the blood plasma 3 h after resuscitation, whereas in the experiments of group 3 the COP level at this time was significantly lower than initially (Table 1). The importance of maintaining the plasma COP in critical states has been noted elsewhere [10].

One of the pathophysiological effects of endogenous toxemia is lowering of the resistance of erythrocyte membranes to hypotonic hemolysis [2]. The most demonstrative results were obtained by the use of 0.7% NaCl. At the 5th minute of the postresuscitation period, when endogenous toxemia was most marked, the degree of erythrocyte hemolysis reached 260% of the initial level, and there were no differences between the groups By the 15th minute after resuscitation

significant differences were found between the experiments of groups 1 and 3: in group 1 the degree of erythrocyte hemolysis was significantly depressed, whereas in group 3 it gradually increased. After 30 min differences were found even compared with group 2, in which injection of pharmacopoieal albumin led to maintenance of the plasma COP, but did not completely abolish the endogenous toxemia. By the 3rd hour, injection of albosorb led to a further reduction of the degree of erythrocyte hemolysis to 141% of the initial value whereas in group 2 the degree of hemolysis was 217% and in group 3 it was 347% of the initial level (Table 1). Consequently, abolition of endogenous toxemia, which most effective if albosorb is used, increases the resistance of erythrocyte membranes to hypotonic hemolysis, and thereby alleviates disturbances of the rheologic properties of the blood.

Analysis of the state of the central hemodynamics showed that treatment with ligand-deprived albumin was accompanied by an increase in the stroke volume of the heart and heart rate compared with the group of untreated animals (group 3), maintaining the volume velocity of the blood flow in the animal at a significantly higher level throughout the 6-hourly period of observation. The cardiac index was 80-128% of the initial value compared with 60-100% in the control (group 3). No significant differences were found in BP, but normalization of the pulmonary arterial pressure in group 1 took place earlier (after 15-30 min). The total oxygen consumption of the animal reached its initial values earlier also (from 15 to 30 min after resuscitation) than in the untreated animals (1 h). This indicated improved ability to utilize oxygen in the tissues, evidently because of increased oxygen transport and reduced disturbance of the microcirculation. Later, moreover, between 1 and 6 h after resuscitation the total oxygen consumption of the animal did not differ significantly from that in the control, despite the more rapid emergence of the treated animals from the state of post-terminal spontaneous hypothermia (Table 1). This state of affairs could contribute to the development of disparity between the existing blood flow and an adequate blood supply necessary for the complete restoration of normal metabolism.

Thus administration of albosorb, with its enhanced detoxicating effect, during the early postresuscitation period increases the binding capacity of the blood plasma relative both to hydrophobic and to hydrophilic molecules, facilitates the early abolition of autointoxication, improves the rheologic properties of the blood and the state of the central hemodynamics, and increases the oxygen supply to and consumption by the body. Albosorb is more effective than pharmacopoieal albumin.

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