POSSIBILITY OF ENTERAL CORRECTION OF POSTHEMORRHAGIC DISTURBANCES DEPENDING ON STATE OF THE ABSORPTIVE FUNCTION OF THE SMALL INTESTINE

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Experimental studies have shown that, in principle, posthemorrhagic hypovolemia responds to enteral infusion therapy [3, 6]. The efficacy of correction is determined by the rapid absorption of the solution entering the small intestine. Information on the state of the absorptive function of the small intestine (AFSI) is therefore essential so that indications for the use of the method of enteral correction of blood loss can be worked out.

We know that the rate of absorption of electrolytes and water remains unchanged after bleeding to the extent of 6% of the circulating blood volume (CBV) [12]. Loss of 25% of CBV increases the ability of the intestine to absorb sodium and water [1, 9, 15]. However, in the case of more severe blood loss, opinions on absorptive function vary: either it is preserved or it is inhibited, or even completely disappears [4]. Morphological studies have shown that the depth of injury to tissue structures of the intestinal mucosa increases with time after rapid massive blood loss [10].

No reference could be found in the accessible literature to the study of the effect of the volume of blood loss and the duration of the posthemorrhagic period on the efficacy of enteral corrective therapy, or to research in which AFSI was studied under conditions most closely resembling natural, at the physiological and morphological levels simultaneously. The investigation described below was carried out for these purposes.

EXPERIMENTAL METHOD

The experimental dogs were prepared by the method in [2] under general anesthesia (the animals were given 0.4 ml of a 2% solution of trimeperidine, 0.5 ml of 0.25% droperidol solution, 0.1 ml of 1% diphenhydramine solution, 0.1 ml of 2.5% chlorpromazine solution, and 1% hexobarbital solution by intravenous drip, per kilogram body weight, until the stage of narcotic sleep). The operation enabled the absorptive function of the small intestine to be studied in a chronic experiment by perfusion of a 50-cm length of it, with blocking of the act of natural digestion during the experiment; biopsy specimens were taken from the mucosa of the small intestine at frequent intervals during the experiment. The experiments with blood loss were conducted under general anesthesia (the animals were given repeated injections of 0.2 ml of 5% calypsol solution, 0.1 ml of 0.5% diazepam (Relanium) solution, and 0.1 ml of 1% diphenhydramine solution per kilogram body weight were given). Blood loss in different volumes (20, 30, 40, and 50 ml/kg) was carried out at the rate of 0.7-1.0 ml/kg · min through a catheter introduced into the aorta via the femoral artery. Either 30 or 60 min after the end of blood loss, enteral correction was carried out with electrolyte-monomer solution [6], and the rate of infusion was controlled by the motor evacuatory function of the intestine. Depending on the difference between the volumes of water and concentrations of components in the perfusion fluids at the entrance to and outlet from the intestine, the rate of absorption of the volume of solution, and of glucose, amino acids, and sodium was calculated per kilogram body weight [2]. The glucose concentration (by the glucose oxidase method), sodium (by flame photome-

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TABLE 1. Characteristics of Absorption of Water, Sodium, Glucose, and Amino Acids in Jejunum 30 min after End of Blood Loss

Group of animals	Rate absorp. on water	Rate of absorp. of total nitro	Rate of absorp. of glucose	Rate of absorption of total nitrogen
	mg/kg·min			
Healthy (n = 30)	0,568±0,024	0,350±0,053	3,67±0,14	1,137±0,053
After blood loss:				
20 ml/kg (n = 20)	0,612±0,060	0,590±0,061*	4,73±0,19*	1,401±0,061*
30-40 ml/kg (n = 18)	0,540±0,054	0,440±0,037	4,88±0,15*	1,392±0,103

Legend. Asterisk indicates that differences compared with initial data (healthy animals) are significant.

TABLE 2. Values of TBV and TVP after Blood Loss of Different Volumes and after Absorption of Electrolyte-Monomer Solution

Group of animals	Vol. of blood loss	CBV	CPV
		ml/kg	
Healthy		79,1±2,0	43,5±1,6
After blood loss	20	65,0±2,0	37,1±1,0
	30	56,4±1,5*	32,2±0,71*
	40	45,1±1,3*	25,7±0,39*
	50	34,2±0,63*	18,8±0,19*
After correction of blood loss	20	80,0±2,4**	53,6±1,8**
	30	70,6±1,9**	48,7±1,4**
	40	65,0±1,6**	47,5±1,6**

Legend. *) Significance of differences compared with initial data, **) with data obtained after blood loss.

try), and total nitrogen (by the Kjeldahl method) were determined in the perfusion fluids by biochemical methods. CBV was determined by the impedance method [8]. The plasma volume of the blood was determined by the hematocrit. The efficacy of enterol correction was assessed on the basis of the values of CBV, CVP, and analysis of mortality. Material for electron-microscopic investigations was fixed in 1% osmic acid solution in phosphate buffer, embedded in Araldite, stained, and examined in the ÉMV-100B electron microscope.

Altogether 108 experiments were carried out on 45 dogs.

EXPERIMENTAL RESULTS

When 30 min had elapsed after the end of blood loss in a volume of 20 ml/kg a significant increase took place in the rate of absorption of amino acids, glucose, and sodium (Table 1). With an increase in the volume of blood loss to 30-40 ml/kg a tendency was observed for the rate of glucose transport to increase still more, whereas the rate of absorption of amino acids was slowed compared with that after loss of 20 ml/kg of blood.

Analysis of the data obtained in these experiments showed that due to preservation of the AFSI, absorption of the solution enabled CBV to be restored (Table 2) and all 100% of the animals subjected to blood loss in a volume of up to 30 ml/kg and 85% of those after blood loss of 40 ml/kg recovered.

The results of experiments in which blood loss amounted to 50 ml/kg revealed marked inhibition of the resorptive activity of the small intestine. Despite intraintestinal infusion of the electrolyte-monomer solution, all the animals died within a few hours of the beginning of the posthemorrhagic period.

Analysis of the results of the morphological investigation showed that structural processes in the intestinal mucosa depended on the volume of blood loss. Moderate edema of the lamina propria of the intestinal villi, smoothing of the epithelium, submembranous edema of the basal portions of the brush-border epitheliocytes (BBE), with discontinuity of the organelles in these zones were found 30 min after a blood loss of 20 ml/kg body weight (Fig. 1a). The ultrastructural study of BBE revealed

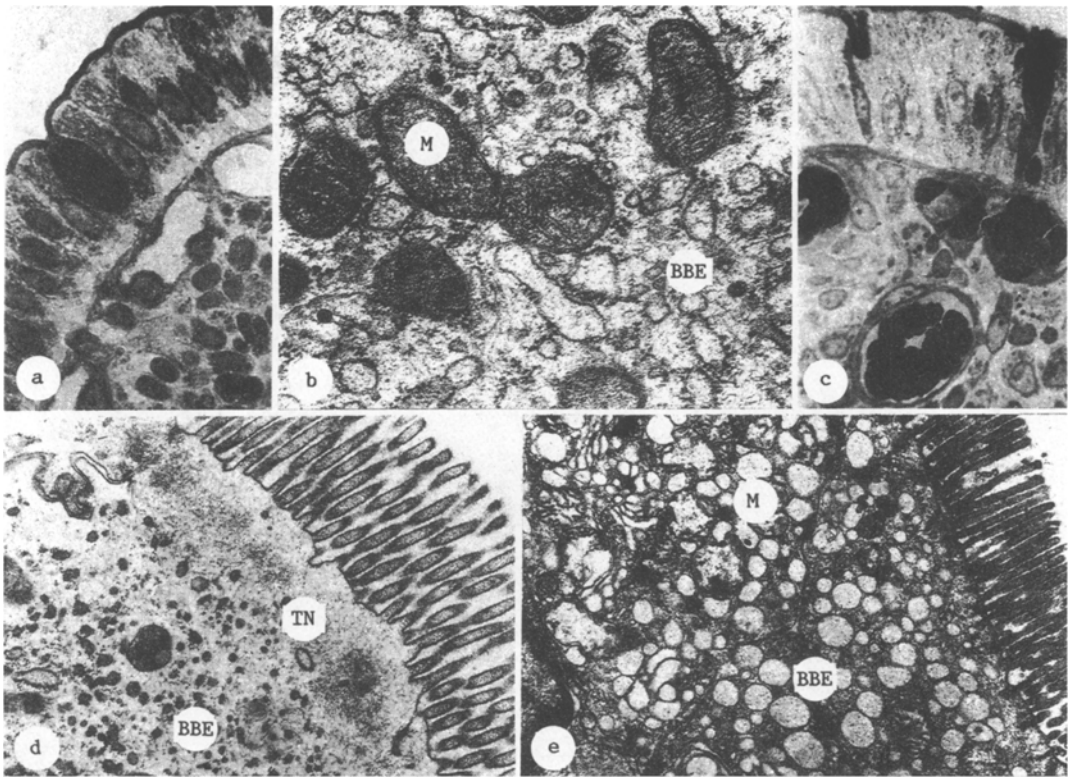

Fig. 1. Histological (a, b) and electron-microscopic (c, d, e) changes in intestinal villi of mucosa of small intestine at different times of the posthemorrhagic period. a) Smoothing of epithelium, edema of cytoplasm of basal portions of BBE. Semithin section. Methyl blue — azure, 900×; b) mitochondria (M) with hyperplasia of cristae. 36,000×; c) erythrocytic aggregates in lumen of subepithelial capillaries. Semithin section. Stained with methyl blue — azure, 900×; d) submembrane edema of BBE, discontinuity of terminal network (TN). 28,000×; e) vacuolation of mitochondria (M) of smooth and rough endoplasmic reticulum of BBE. 20,000×.

signs of tissue hypoxia and associated compensatory activation of the organelles (moderate hypertrophy of the mitochondria, hyperplasia of the cristae, and dilatation of cisterns of the rough endoplasmic reticulum (Fig. 1b).

An increase in the volume of blood loss to 30-40 ml/kg was accompanied by a decrease in thickness of the brush border (BBE), by narrowing of the intercellular spaces, and by even more marked compensatory hypertrophy of the organelles responsible for absorption. Other data, in agreement with the results of investigations by other workers, indicate that morphologically expressed inhibition of the absorptive function took place after blood loss of 50 ml/kg, when the increasing degenerative changes in the absorptive epithelium led to denudation of many villi and prevented effective enteral correction of blood loss of this magnitude.

According to the results of the morphological investigations, 30 min after the end of infusion of the solution the state of the subepithelial capillaries, arterioles, venules, and lymphatics and also of the organelles and cytoplasm of BBE demonstrated active resorption without any strain on intracellular metabolism after blood loss of 20 ml/kg (Fig. 2a, b) and with strain on fluid transport after blood loss of 30-40 ml/kg (Fig. 2c, d). Next day the absorptive epithelium and capillaries of the intestine did not differ from their initial normal state (Fig. 2e).

The study of the efficacy of enteral infusion therapy in the late period after blood loss showed that after blood loss of 20 ml/kg the absorptive function was independent of the duration of the posthemorrhagic period, and after enteral infusion of the solution all the animals recovered. However, with an increase in the volume of blood loss this dependence appeared. Inhibition of AFSI, expressed individually to a greater or lesser degree, developed after 60 min of the posthemorrhagic period and determined the outcome of enteral correction (after blood loss of 30 ml/kg 30% of the animals died, but 50% after blood loss of 40 ml/kg).

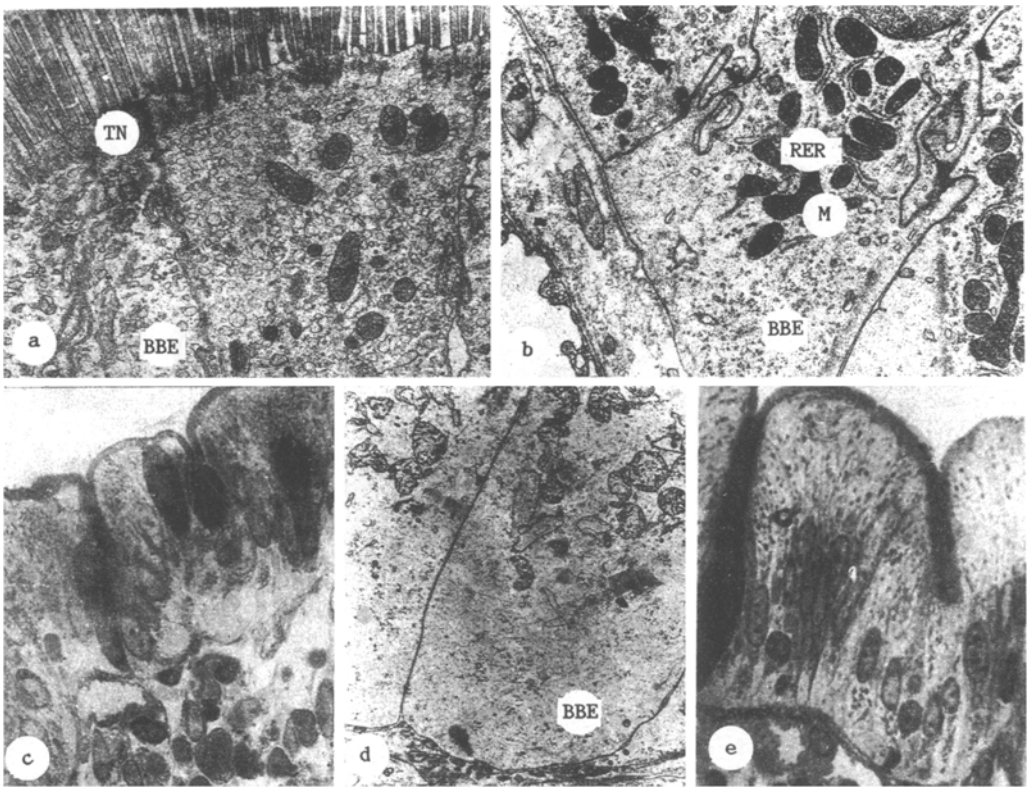

Fig. 2. Histological (c, e) and electron-microscopic (a, b, d) changes in intestinal villi of mucous membrane of small intestine after correction of blood loss: a) numerous microvesicles in cytoplasm of BBE, preservation of terminal network (TN), 20,000×; b) mitochondria (M), polysomes, and cisterns of rough endoplasmic reticulum (RER) in cytoplasm of basal portions of BBE. 20,000×; c) edema of lamina propria of intestinal villi and basal portions of cytoplasm of BBE. Semithin section. Methyl blue — azure, 900×; d) discontinuity of organelles of cytoplasm of BBE. Submembranous edema, 22,000×; e) high cylindrical epithelium of intestinal villi with well marked brush border. Semithin section. Methyl blue — azure, 900×.

Histological investigations of the mucosa of the small intestine 60-90 min after blood loss of 20 ml/kg caused increasing signs of intracellular edema. The intravascular changes, in the form of congestion of the capillaries and aggregation of erythrocytes, progressed (Fig. 1c). After blood loss of greater volume the morphological changes depended even more on the duration of the posthemorrhagic period. Thinning and disappearance of the glycocalyx on the surface of the microvilli, vacuolation of the smooth and rough endoplasmic reticulum, swelling of the mitochondria, and lysis of their cristae were observed in BBE in the electron microscope. As a result of the cellular hypoxia the degenerative changes in the absorptive epithelium were intensified, often with the formation of microerosions and with partial desquamation of the intestinal villi at their apices, which could restrict AFSI (Fig. 1d, e).

Comparison of the results of the physiological and morphological investigations of AFSI showed that despite the increasing circulatory, structural, and metabolic changes increasing in severity with an increase in the volume of blood loss to 30-40 mg/kg, inhibition of absorptive function was not observed during the next 30 min. Its preservation under hypovolemic conditions could be due to the stabilization of the mesenteric blood flow, observed in our morphological investigations, as a result of its autoregulation [7], after the entry of food monomers into the intestinal lumen [14], which together ensure an adequate blood supply to the intestine and its enhanced absorptive activity in the immediate posthemorrhagic period.

The acceleration of glucose consumption observed in these experiments may have been due to an increasing deficit of the supply of energy for the transporting function of the small intestine, due to the morphologically evident circulatory hypoxia. As a result, some glucose was metabolized in the intestinal wall and supplied energy for adequate absorption of water, monomers, and electrolysis [11, 13]. Indirect evidence in support of this conclusion was given by activity of mitochondria, revealed by

electron-microscopic investigations, and whose functions, according to our own data and observations in the literature, increased with an increase in the volume of blood loss [5].

Analysis of the experimental data showed that disturbances of AFSI, varying in degree depending on the individual resistance of the animals to circulatory-anemic hypoxia [5], develop in 30-50% of animals after blood loss in a volume of 3040 ml toward the end of the first hour and make effective enteral correction of posthemorrhagic complications impossible. Enteral correction in that case is sufficient to maintain the animal's life when it begins in the immediate period after blood loss, i.e., 30 min after blood loss of 30-40 ml/kg or 90 min after blood loss in a volume of 20 ml/kg. In the other case, it can be regarded as an active component in a program of therapeutic measures.

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