WATER, SODIUM, AND POTASSIUM CONTENT IN THE TISSUES OF RATS WITH CIRCULATORY FAILURE DUE TO CONSTRICTION OF THE THORACIC PORTION OF THE INFERIOR VENA CAVA

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KEY WORDS: circulatory failure; edema; muscle; liver; sodium; potassium.

Disturbance of the regulation of Na^+ and water metabolism during circulatory failure is manifested as reduced ability of the kidneys to excrete NaCl solution introduced into the body [6]. The writers showed previously [2] that during edema formation rats excrete urine with a low Na^+ concentration. Since rats by preference drink 0.9% NaCl solution during edema formation and since the Na^+ concentration in the urine is much lower than in the blood plasma, it will be evident that relatively more Na^+ than water is retained in the body of edematous rats. The question of the possible retention of Na^+ in the tissues and its role in the pathogenesis of edema has not yet been adequately studied.

The object of this investigation was to study the content of water and the principal cations (Na^+ and K^+) in the tissues of edematous rats with experimental circulatory failure. Muscle tissue, which accounts for a considerable part of the dry substance of the body, and the liver, because edema was caused by constriction of the vena cava and was accompanied by disturbance of the outflow of blood from the liver, were chosen as the test objects.

EXPERIMENTAL METHOD

Circulatory failure was induced in rats by application of a ring to the inferior vena cava by the method described in [2]. Only edematous animals, whose gain in weight 1-2 days after application of the ring was not less than 10% of their initial weight, were studied in the experimental group. The mean body weight of the rats before operation was 360 g and after the operation 450 g. A mock operation, pneumothorax without application of the ring, was performed on some of the control animals.

The rats were anesthetized with ether and decapitated to obtain blood samples. At autopsy on the animals pieces (30-80 mg) of the rectus abdominis muscle and liver were excised. The content of water and of Na^+ and K^+ ions in the tissues was determined [3].

EXPERIMENTAL RESULTS

The content of water and Na^+ and K^+ ions in the tissues of rats undergoing the mock operation and control rats did not differ significantly, and the data for these groups were accordingly pooled as the control. Compared with animals of the control group, the content of water and Na^+, calculated per unit wet weight (Table 1), was considerably increased in the muscle tissue and liver of the edematous rats. Since the proportion of dry substance in the test tissues was reduced in the edematous animals, a relatively larger increase also was observed in the water and Na^+ content calculated per unit dry weight of muscle and liver (Table 2). Conversely, the K^+ concentration in the tissues of the edematous rats was reduced when calculated per wet weight, but did not differ from the control when calculated per dry weight of muscle and liver.

The increase in the water content in the test tissues was evidently the result of the increase in their extracellular volume, because the increase in the total water content of

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TABLE 1. Content of Water (in g) and Sodium and Potassium (in μeq) per Gram Wet Weight of Tissue (M ± m)

Experimental conditions	Muscle				Liver			
	H_2O	Na^+	K^+	$Na^+ + K^+$	H_2O	Na^+	K^+	$Na^+ + K^+$
Control	0,734±0,006	28,0±1,2	101,0±1,1	131±2,0	0,705±0,003	25,7±1,0	102,1±1,3	128±1,5
	($n = 30$)				($n = 21$)			
Edema	0,780±0,004 †	50,2±1,7†	86,0±1,8†	136±1,2 *	0,753±0,003†	52,5±2,8†	84,0±3,0†	137±2,3†
	($n = 43$)				($n = 21$)			

*P < 0.05.
†P < 0.001.

TABLE 2. Content of Water (in g) and of Sodium and Potassium (in μeq) per Gram Dry Weight of Tissue (M ± m)

Experimental conditions	Muscle			Liver		
	H_2O	Na^+	K^+	H_2O	Na^+	K^+
Control	2,84±0,07	106,8±5,1	394±11	2,36±0,03	87,3±3,1	343±6.2
		$n = 30$			$n = 21$	
Edema	3,62±0,08*	230±7,9*	391±9,4	3,09±0,04*	214±13*	396±10
		$n = 43$			$n = 31$	

*P < 0.001.

the body of the edematous rats was the same as the increase in the extracellular space and the gain in body weight [1, 2]. Investigations on isolated tissues also show that mammalian cells have well-marked ability to regulate their own volume, even during considerable changes in the composition of the external medium [13]. Expansion of the extracellular volume can lead to changes in the ionic composition of the tissues, for the Na^+ concentration in the interstitial fluid is much higher, and the K^+ concentration lower, than the intracellular concentration of these ions. Assuming that the increase in the quantity of water in the tissues of the edematous rats took place on account of expansion of the extracellular space, the addition of the extracellular fluid to the tissues amounted on average to 0.05 ml/g wet weight (Table 1), in that case the quantity of Na^+ per gram wet weight ought to have increased by 7 μeq, whereas the Na^+ concentration in the interstitial fluid was only 140 μeq/ml. The quantity of K^+ in the tissues after the addition of the same volume of extracellular fluid ought to have reduced its concentration in the wet tissue by not more than 5%, because the quantity of added K^+ was immeasurably small compared with its intracellular content. Comparison of these calculated data with the values actually obtained, and given in Table 1, shows that the increase in the Na^+ content and decrease in the K^+ level in muscle and liver tissues were considerably greater than can be accounted for on the basis of an increase in the quantity of extracellular fluid in the tissues of the edematous animals. It can be tentatively suggested that the intracellular content of both Na^+ and K^+ changes during the development of edema.

This hypothesis is supported by the results of analysis of the relationship between the Na^+ and K^+ concentrations in the test tissues. In healthy animals the tissues are characterized by relative stability of the Na^+ and K^+ concentrations and by absence of correlation between the concentrations of these ions (Figs. 1 and 2). A high degree of negative correlation was observed in the edematous rats between the Na^+ and K^+ concentrations in muscles ($r = -0.57$); $P < 0.01$) and liver ($r = -0.61$; $P < 0.01$). It can be postulated that some of the intracellular K^+ in the muscle and liver of the edematous rats was exchanged for Na^+ in the ratio of 2:3. A small but statistically significant increase in the total content

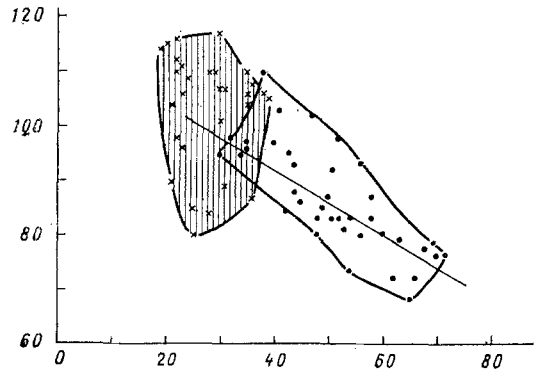

Fig. 1

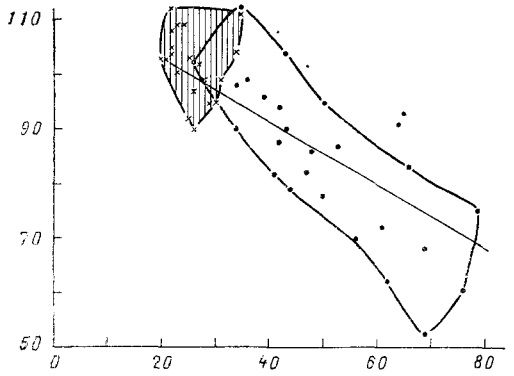

Fig. 2

Fig. 1. Relationship between Na^+ and K^+ concentrations in muscle of control (crosses) and edematous (dots) rats. Abscissa, Na^+ concentration in muscle (in μeq/g wet weight); ordinate, K^+ concentration in muscle (in μeq/g wet weight). Shaded zone — data obtained on control animals. Straight line is regression line $[K^+] = 116 - 0.60\ [Na^+]$.

Fig. 2. Relationship between Na^+ and K^+ concentrations in liver of control (crosses) and edematous (dots). Straight line represents regression line $[K^+] = 115 - 0.58\ [Na^+]$. Legend as to Fig. 1.

of Na^+ and K^+ in the tissues was observed in the edematous animals (Table 1), possible evidence of an increase in the fraction of Na^+ bound with structural components of the cell. As many workers have shown, a high proportion of the Na^+ in the cell is in a bound state and exchange for K^+ can take place on account of the bound form [5, 12].

This conclusion regarding accumulation of Na^+ in the cells and loss of K^+ in rats with edema, caused by constriction of the intrathoracic part of the inferior vena cava, is in agreement with the results of investigation of the distribution of isotopes ^{22}Na and ^{42}K in patients with edema [8, 10, 14]. Besides retention of Na^+ in these patients, a decrease in the K^+ concentration in the body also is observed. Similar changes in the ionic composition of muscle tissue also occur in certain other diseases [7, 10, 15]. Many investigations on isolated muscle fibers and other tissues have shown accumulation of Na^+ in the cells in exchange for K^+ in response to various factors: a fall in ambient temperature, hypoxia, administration of respiratory inhibitors, etc. [4, 13].

Since circulatory failure is accompanied by marked tissue hypoxia, it can be postulated that in edematous rats a "pump failure" arises in the muscle and parenchymatous cells, as is observed in ischemic zones of the myocardium [11]. "Failure of the sodium pump" has been suggested as the explanation of disturbance of Na^+ and K^+ metabolism in man during chronic bronchospasm [15]. It can be tentatively suggested that in tissue hypoxia activity of the enzyme system responsible for Na^+ transport against the gradient is reduced, and this leads to retention of Na^+ in the cell.

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PLASMA PROTEIN SPECTRUM OF DOGS TREATED FOR HYPOXIA WITH THE SEVER-OMR MEMBRANE OXYGENATOR

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Membrane oxygenators (MO), instruments for nonpulmonary gas exchange, have become increasingly widely used for the treatment of hypoxic states in recent years. When their basic working parameters (gas-exchange properties) are studied, the need arises for assessment of the side effects of the foreign-body surfaces of the MO on the protein composition of the blood. Meanwhile, comparatively little is known about the character of the denaturation changes in blood plasma proteins due to prolonged operation of extracorporeal systems with MO [1, 6, 8]. It must be emphasized that the plasma protein spectrum of dogs — widely used experimental animals — obtained by electrophoresis on polyacrylamide gel (PAG) has received very little study.

The object of this investigation was to study the effect of the Sever-OMR MO on the blood protein spectrum of dogs during treatment for respiratory failure.

EXPERIMENTAL METHOD

Experiments were carried out on 12 mongrel dogs of both sexes weighing 18-22 kg, under morphine–hexobarbital anesthesia, using succinylcholine as muscle relaxant and artificial ventilation, under hypoventilation conditions (respiration rate 3-4 cycles/min, respiratory minute volume 40% of normal). For therapeutic purposes, for extrapulmonary additional gas exchange, the Sever-OMR MO was connected to an arteriovenous shunt formed on the femoral vessels. Artificial pumps were not used. The normal body temperature of the animals was maintained by an external heater. The volume velocity of the blood flow through the shunt was 800-1100 ml/min. The dose of heparin was 8-10 mg/kg (initial dose), followed by further injections of the anticoagulant under control of the activated blood clotting time.

The protein composition of the blood plasma was determined by electrophoresis on PAG [4] in blood samples taken from dogs in the initial state (after induction of anesthesia, during spontaneous respiration) and after prolonged (2.5-3 h) treatment for hypoventilation hypoxia by extrapulmonary gas exchange in the Sever-OMR MO. The data were analyzed visually and densitometrically (with a densitometer from Zeiss, East Germany, with attachment for a cylindrical gel). The number and relative position of the individual fractions were determined visually. The R_f values for each fraction relative to transferring, taken as 1, were determined from the densitogram.

EXPERIMENTAL RESULTS

By electrophoresis on PAG human blood plasma proteins can be divided into 20 or more fractions [4]. After partial or total denaturation of the protein molecule its quaternary

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