CHANGES IN THE TOTAL RNA AND DNA CONTENTS IN THE BRAIN AND VISCERA (LIVER AND HEART) AFTER PROLONGED HYPOVOLEMIC HYPOTENSION AND IN THE POSTRESUSCITATION PERIOD

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The importance of research into nucleic acid metabolism to the study of the mechanism of hypoxic damage to the brain and viscera has been demonstrated by several workers [2, 3, 7]. Determination of the character of changes in nucleic acids in the posthypoxic period appears particularly important, for it is in that period that morphological lesions are formed in animals resuscitated from the terminal state [4-6, 8, 9].

The object of this investigation was to study changes in the total RNA and DNA contents in the gray matter of the cerebral cortex, the liver, and heart during hypovolemic hypotension lasting 4 h and at various stages of the postresuscitation period.

EXPERIMENTAL METHOD

Experiments were carried out on 43 dogs of both sexes weighing 11-22 kg. Under superficial pentobarbital anesthesia with Pantopon or trimeperidine premedication (4-8 mg/kg body weight) the animals were subjected to rapid (in the course of 5-8 min) bleeding from the femoral artery, reducing the arterial blood pressure (BP) on average to 40 mm Hg, and maintaining it at this level for 4 h. The total blood loss amounted to 40 ± 5 ml/kg. BP was restored by fractional intraarterial injection of the collected blood into the femoral artery initially, and later intravenously. Dextran was injected by intravenous drip immediately after reinfusion of the blood [1].

Brain tissue for biochemical tests was obtained by intravital punch biopsy through a burr-hole under thiopental anesthesia (10-20 mg/kg): immediately after the burr-hole was drilled (control group) after 4 h of hypovolemic hypotension, and 1 h, 14-21 days, and 3-4 months after beginning of the postresuscitation period (experimental group). Liver and myocardial (left ventricle) tissue was obtained from animals killed by electrocution (127 V).

The total RNA and DNA content was determined in homogenates of the gray matter of the cortex, liver, and myocardium [10].

EXPERIMENTAL RESULTS

As Table 1 shows the total RNA content in the gray matter of the cortex by the 4th hour of hypotension was reduced by 4.2 mg% ($P < 0.05$). The total RNA level remained low for 3-4 months after resuscitation, despite a tendency towards normalization observed on the 14th-21st days of the postresuscitation period. Consequently, not only during lethal exsanguination, but also during a long postresuscitation period the total RNA level in the cerebral cortex remained depressed, so that biosynthetic activity in the nerve tissue was reduced and structural metabolism of the brain was retarded in the postresuscitation period. If the total RNA content in the cerebral cortex was 6.7 ± 0.3 mg% in the immediate postresuscitation period, i.e., it was reduced by about 50% compared with the control, complete neurologic recovery did not take place in these dogs (behavioral reactions and static posture were disturbed, trophic ulcers appeared in the skin). The sharp fall in synthetic activity in ani-

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TABLE 1. Changes in Nucleic Acid Content (in mg%) in Tissues of Brain Gray Matter, Liver, and Myocardium after 4 h of Hypovolemic Hypertension and in Postresuscitation Period (M ± m)

Test object	Control		Hypotension		Postresuscitation period					
					1 h		2—3 weeks		3—4 months	
	RNA	DNA	RNA	DNA	RNA	DNA	RNA	DNA	RNA	DNA
Brain	11,2±0,7 (8)	5,4±0,3 (8)	7,0±0,3* (6)	5,2±0,1 (6)	6,7±0,3* (6)	5,0±0,2 (6)	8,4±0,4* (6)	4,5±0,2* (6)	9,1±0,3* (7)	4,1±0,2* (7)
Myocardium	14,2±1,8 (9)	10,5±0,4 (9)	8,2±0,2* (6)	10,0±0,2 (6)	9,4±0,4* (7)	10,3±0,3 (7)	13,7±1,3 (6)	11,4±0,9 (6)	16,3±1,6 (9)	11,2±1,6 (9)
Liver	43,5±2,2 (9)	18,6±0,4 (9)	38,4±0,7* (6)	16,8±0,5* (6)	37,3±0,5* (7)	16,6±0,4* (7)	35,7±1,1* (6)	16,5±0,7* (6)	42,7±1,9 (9)	19,5±0,7 (9)

Legend: 1) *P < 0.05 compared with control; 2) number of experiments given in parentheses.

mals with disturbed recovery of CNS functions, when the total RNA content was 1.7 mg% lower ($P < 0.05$) than in animals with complete recovery of CNS functions, evidently aggravated the course of the postresuscitation period. It can be tentatively suggested that restoration of CNS functions in the postresuscitation period is closely linked with the capacity for intracellular synthesis and accumulation of nucleic acids.

The DNA content in the cerebral cortex remained unchanged during hypovolemic hypotension and the early postresuscitation period (Table 1). These observations show, first, that DNA is resistant to hypoxia and ischemia and, second, that damage to nerve tissue under these conditions is limited. As Table 1 shows, a significant decrease in DNA took place on the 14th-21st day of the postresuscitation period. Consequently, these changes were delayed in character. No significant differences were found in the DNA content of the gray matter of the brain in animals with outwardly complete and incomplete recovery of CNS functions: 4.5 ± 0.2 and 4.3 ± 0.3 mg% respectively.

Comparison of the trend of the total RNA and DNA contents in the cerebral cortex during the terminal process and after resuscitation showed that soon (14-21st days) and in the late stages (3-4 months) after resuscitation biosynthetic processes were activated. This was linked with a rise in the total RNA level. Areas of necrosis with involvement of nerve cell nuclei in the pathological process formed simultaneously [2]. However, this apparently divergent dynamics of the total RNA and DNA content reflected the particular features of the postresuscitation period, when predominance of pathological destructive reactions determines the depth of postresuscitation brain pathology.

Comparison of changes in the DNA content in the brain, liver, and myocardium revealed an earlier decrease in liver tissue (by 1.8 mg%; $P < 0.05$) — still in the period of hypotension (Table 1). Conversely, the DNA content in the myocardium was resistant to the action of harmful factors both during the terminal process and in the postresuscitation period.

Significant differences also were found in the rates of recovery of the nucleic acid content in tissues of the brain and viscera. For instance, whereas the nucleic acid content in liver tissue was back to normal by the 3rd or 4th month after resuscitation, recovery of total RNA in the myocardium took place much more rapidly (by the 14th-21st day). Unlike in the viscera, the total RNA and DNA content in the cerebral cortex did not regain its initial levels until more than 3-4 months after the beginning of the postresuscitation period.

In the case of incomplete recovery of CNS functions in animals exposed to hypovolemic hypotension for 4 h the total RNA content in the liver tissue was 34.3 ± 0.9 mg%, i.e., it was 8.4 mg% lower ($P < 0.05$) than in animals with outwardly complete neurological recovery. This is evidence of more profound changes in structural metabolism of the liver cells when the neurological status is disturbed.

Considerable disturbances of nucleic acid metabolism in the CNS and viscera, continuing for a long time into the postresuscitation period, can thus lead to insufficiency of regenerative and repair processes after acute blood loss. Disturbance of these processes may play the dominant role in the formation of irreversible postresuscitation changes after acutely developing terminal states.

LITERATURE CITED

1. V. L. Kozhura, Byull. Eksp. Biol. Med., No. 10, 39 (1975).
2. V. L. Kozhura, G. N. Mirotvorskaya, L. V. Molchanova, et al., Anesteziol. Reanimatol., No. 3, 61 (1979).
3. E. M. Kreps, in: Physiology and Pathology of Respiration, Hypoxia, and Oxygen Therapy [in Russian], Kiev (1958), pp. 40-45.
4. V. A. Negovskii, Current Problems in Resuscitation [in Russian], Moscow (1971).
5. V. A. Negovskii, A. M. Gurvich, and E. S. Zolotokrylina, Postresuscitation Sickness [in Russian], Moscow (1979).
6. N. K. Permyakov, Fundamentals of Resuscitation Pathology [in Russian], Moscow (1979).
7. I. M. Tyrmyshnikov, "Nucleic acid metabolism in the brain, liver, and other viscera during hyperbaric oxygen therapy after massive acute blood loss," Author's Abstract of Doctoral Dissertation, Voronezh (1974).
8. J. H. Adams, Br. J. Anaesth., 47, 121 (1975).
9. J. B. Brierley, A. W. Brown, B. J. Excell, et al., Brain Res., 13, 68 (1969).
10. C. Schmidt and A. Thannhauser, J. Biol. Chem., 161, 83 (1945).