DYNAMICS OF NUCLEIC ACID CONTENT IN THE LIVER DURING LETHAL BLOOD LOSS ASSOCIATED WITH PROLONGED HYPOTENSION AND DURING RECOVERY FROM CLINICAL DEATH

V. L. Kozhura

UDC 616-005.1-036.882-07:616.36-008.939.332-074

In experiments on dogs the dynamics of the nucleic acid concentration in the liver was studied during lethal blood loss associated with prolonged hypotension (50-30 mm Hg) and in the recovery period after clinical death for 1-2 min. At the end of the second hour of hypotension a marked decrease in the RNA and DNA concentrations was observed in the liver. In the recovery period the concentration of nucleic acids continued to fall. On the 5th-6th day a marked tendency for the nucleic acid level in the liver of the surviving animals to return to normal was observed.

* * *

The role of the nucleic acids in the liver is extremely important because of the high intensity of their metabolism and the high mobility of synthetic processes in the liver. In the present investigation, the dynamics of the RNA and DNA content in the liver was studied in dogs during protracted lethal blood loss and in the recovery period after clinical death. Disturbances of the structure and function of the liver have often determined the outcome of subsequent resuscitation [3].

EXPERIMENTAL METHOD

Experiments were carried out on 28 dogs of both sexes weighing 10-25 kg. Investigations on 12 of these animals were carried out only in the initial state.

As a model of the terminal state, acute blood loss preceded by hypotension (50-30 mm Hg) for 1.5-2 h was used. It was maintained by slow exsanguination or by intraarterial injection of small volumes of blood.

After clinical death lasting 1-2 min the animals were resuscitated by Negovskii's method [2].

Liver tissue obtained by open punch biopsy was investigated at the following stages of the experiment: in the initial state, after hypotension for 1-2 h, 30 min, and 3 and 9 h after resuscitation, and on the 5th-6th day in the surviving animals.

The liver biopsy material was dried on filter paper, traces of blood were removed, and the material was weighed (8-12 mg tissue) and placed in a glass microhomogenizer with Teflon pestle containing 0.8 ml of a 2:1 mixture of chloroform and ethanol, and homogenized in the cold for 3-5 min. The lipid and acid-soluble fractions and the phosphorus-containing components of lipoproteins were then removed from the homogenate [1]. The nucleic acids were separated by a modified method of Ogur and Rozen [1]. Phosphorus of RNA and DNA, from which the concentrations of the nucleic acids in the liver was judged, was determined quantitatively by ultraviolet spectrophotometry [7].

EXPERIMENTAL RESULTS

The volume of blood lost to cause clinical death was ($M \pm \sigma$) 59±18% of the total blood volume of the animal.

Laboratory of Experimental Physiology of Resuscitation, Academy of Medical Sciences of the USSR, Moscow. (Presented by Active Member of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 3, pp. 46-48, March, 1969. Original article submitted April 18, 1968.

TABLE 1. Concentration of Nucleic Acids (mg% phosphorus of fresh tissue) in Liver of Dogs Dying from Blood Loss against a Background of Prolonged Hypotension and during Recovery Period after Clinical Death ($M \pm \sigma$)

Index	Original state	Hypotension		Recovery period		
		1 h	1.5-2h	30 min	3 h	9 h
RNA concentration	30,3±1,4 (23)	27,5±2,0 (11)	22,7±2,2[1] (11)	20,0±1,6[1] (12)	16,5±1,0[1] (11)	16,7±1,5[1] (10)
DNA concentration	17,6±0,6 (23)	16,8±1,1 (11)	14,8±0,9[1] (11)	13,5±0,7[1] (12)	12,6±0,7[1] (11)	12,1±0,5[1] (10)

*P < 0.01-0.05 relative to original value. Number of observations in parentheses.

The cardiac activity was restored in most experiments 15-55 sec after the beginning of resuscitation; in the experiments in which ventricular fibrillation developed it was restored after a period of between 55 sec and 8 min 20 sec. Spontaneous respiration reappeared after 1-9 min. Four of the 16 dogs survived and in 3 of them the vital functions were fully restored. The remaining animals died at various time during the recovery period (ranging from a few hours to 4 days).

The results in Table 1 show that the RNA concentration in the liver after hypotension for 1 h showed a tendency to diminish, and this tendency became significant after 2 h. In the recovery period, the RNA concentration in the liver continued to fall after resuscitation of the animals.

In the animals which died the RNA phosphorus concentration in the liver by the 9th hour of the recovery period was 13.6±1.0 mg%, compared with 21.4±0.8 mg% for the surviving animals. On the 5th-6th day after resuscitation, the RNA level in the liver of this group of animals showed a marked tendency toward returning to normal.

The DNA concentration in the liver was significantly lowered after hypotension for 2 h. In the recovery period after clinical death a further decrease in the DNA concentration in the liver cells was observed. The DNA phosphorus concentration 9 h after resuscitation in the liver of the animals which died was 10.9±0.5 mg%, and 13.9±0.9 mg% in the survivors. On the 5th-6th day the DNA concentration in the liver of the surviving animals was identical with the initial values.

The decrease in the RNA and DNA concentrations in the liver of animals during prolonged lethal blood loss and after resuscitation coincided in time with degenerative changes, frequently irreversible, in this important parenchymatous organ [4, 8]. A study of liver function during prolonged lethal exsanguination and in the postresuscitation period has revealed considerable disturbances of proteinogenic, prothrombinogenic, excretory, and other hepatic functions [5, 6]. It may be postulated that the disturbance of liver function during the terminal process and the postresuscitation period is closely connected with changes in metabolism of nucleic acids and other macromolecular compounds.

The decrease in the RNA and DNA concentrations in the liver during prolonged lethal blood loss and in the recovery period after clinical death points to a profound disturbance of the ability of the liver to provide structural materials in animals in a terminal state and after resuscitation.

LITERATURE CITED

1. M. I. Baranov, Biokhimiya, No. 4, 702 (1962).
2. V. A. Negovskii, Pathophysiology and Treatment of Agony and Clinical Death [in Russian], Moscow (1954).
3. V. A. Negovskii, A. M. Gurvich, E. S. Zolotokrylina, et al., in: Shock and Terminal States [in Russian], Leningrad (1960), p. 82.
4. N. P. Romanova, in: Fundamentals of Reanimatology [in Russian], Moscow (1966), p. 235.
5. V. M. Shapiro, Pat. Fiziol., No. 3, 32 (1966).
6. V. M. Shapiro, Pat. Fiziol., No. 4, 40 (1967).

7. R. G. Tsanev and G. G. Markov, Biokhimiya, No. 1, 151 (1960).
8. T. Ichioka, Kobe J. Med. Sci., 4, 1 (1958).