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DYNAMICS OF STRUCTURAL METABOLISM IN THE LIVER DURING HYPERBARIC OXYGENATION IN THE RECOVERY PERIOD AFTER ACUTE MASSIVE BLOOD LOSS

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An important role in the course and outcome of terminal and other hypoxic states has been shown to be played by changes in nucleic acid metabolism in the liver [3, 5, 6, 14, 15]. Profound disturbances of nucleic acid metabolism in the liver have a definite effect on formation of irreversible changes after massive blood loss [5, 14, 15]. The development of a terminal state (agony) after acute massive blood loss is accompanied by inhibition of synthesis of nuclear and cytoplasmic RNA and by a fall in the concentrations of both RNA and DNA in the liver tissue. The wide use of hyperbaric oxygenation (HBO) in the treatment and prevention of hypoxic states [2, 12] has necessitated the study of its effect on the dynamics of metabolism of highly important biopolymers in the liver tissues and on the outcome of severe hypoxic states. It has been shown that oxygen, given by HBO, has a varied effect on nucleic acid metabolism in the tissues [4, 7, 12, 14, 15]. The amplitude of the oxygen effect is known to be extremely wide. On the one hand, it may lead to severe poisoning, on the other hand it may give a powerful therapeutic effect [8, 12]. The biological effect of oxygen depends both on the conditions of HBO and on the state of the patient or animal treated with oxygen. Experimental data and clinical observations show that HBO has different effects on the healthy organism and in pathology accompanied by hypoxia [8, 12]. It has been shown experimentally that when healthy animals are subjected to HBO, profound disturbances of nucleic acid metabolism are observed in the tissues, and are expressed as increased activity of lysosomal enzymes (RNase, DNase) and a fall in nucleic acid concentrations in the tissues [7]. As a result of exposure of a healthy organism to hyperbaric oxygenation, the regenerative activity of the cells is depressed [8]. The use of HBO in the early stages after acute massive blood loss has been shown to prevent the inhibition of synthesis of nuclear and cytoplasmic RNA, the fall in the nucleic acid (RNA and DNA) concentrations, and also the development of a terminal state in most animals [14, 15]. However, the effect of HBO on nucleic acid and protein metabolism in the liver has not been studied in the recovery period after massive blood loss, yet this is important for an understanding of the pathogenesis of complications which develop in the postresuscitation period, in which disturbances of nucleic acid and protein metabolism in the tissues play an important role [6, 11].

This paper describes a study of the effect of HBO on structural metabolism in the liver in the recovery period after acute massive unreplaced blood loss.

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TABLE 1. Effect of HBO on Structural Metabolism in the Liver in the Recovery Period after Acute Massive Blood Loss

Group of animals	Concentration, mg% in wet tissue		Specific radioactivity, Bq/ml	
	RNA	DNA	RNA	Protein
1 (control)	414±19,4	215±5,6	483±13,3	13,7±0,26
2	307±12,3*	193±6,1*	373±20,3*	9,6±0,26*
3	404±12,5	213±10,7	451±19,7	12,5±1,6
immediately after HBO				
after blood loss				
2nd day	385±8,3*	229±22,9	658±10,2*	14,5±0,17
4th day	443±5,7	213±6,3	702±9,1*	16,8±0,37*
8th day	465±19,3*	213±8,6	604±13,7*	17,2±0,68*
15th day	488±10,3	227±9,6	573±65,5*	15,8±0,18*
4th according to scheme in text				
2nd day	443±5,8**	205±9,8	985±36,0**	25,0±2,8**
4th day	530±8,6**	252±0,5**	864±51,1**	24,9±3,1**
8th day	535±8,7**	219±6,3	776±47,5**	16,3±2,5
15th day	450±8,3	219±3,6	488±55,3	14,6±3,9

Legend. *)Significance of differences compared with control, **) compared with animals receiving one session of HBO.

EXPERIMENTAL METHOD

Experiments were carried out on 302 albino rats of both sexes weighing 195-205 g and divided into four groups. Intact animals formed group 1 (control). Group 2 consisted of animals which developed a terminal state (agony) after blood loss. Animals of group 3 were subjected to a single session of HBO after blood loss and then decapitated at different times in the recovery period. In the animals of group 4 HBO was used both immediately after blood loss and in the course of the recovery period, in accordance with the following scheme. On the 1st day after blood loss HBO was given for 60 min at 3 atm (3039 hPa), again 12 h later for 30 min at 2 atm (2026 hPa), and after an interval (10 min) HBO was repeated for 30 min at 2 atm (2026 hPa). On the 2nd day HBO was given for 30 min at 2 atm (2026 hPa), and repeated after an interval of 10 min for 30 min at 2 atm (2026 hPa). On the 3rd day HBO was given for 30 min at 1.5 atm (1519 hPa) and again, after an interval of 10 min, for 30 min at 1.5 atm (1519 hPa). On the 4th day the program was the same as on the 3rd day. On the 5th day HBO was given for 25 min at 1.5 atm (1519 hPa), and again after an interval of 10 min for 20 min at 1.5 atm (1519 hPa). The program on the 8th day was the same as on the 5th day. On the 10th day HBO was given for 40 min at 1.0 atm (1013 hPa). The program on the 12th day was the same as on the 10th day. On the 15th day HBO was given for 40 min at 0.5 atm (506 hPa). By giving HBO in accordance with this scheme, the toxic action of oxygen was avoided. In the region of exposure of the vein, the tissue was infiltrated with 0.5 ml of 0.5% procaine. Bleeding was carried out from the right jugular vein in a volume of 3.5% of body weight in the course of 30 min. During the study of total RNA synthesis, ^{3}H-orotic acid was injected intraperitoneally 60 min before decapitation in a dose of 30 μCi/100 g body weight. In these experiments RNA was isolated from the tissues by the hot phenolic method [1]. Total protein synthesis was investigated by the use of a ^{14}C-labeled amino-acid digest of chlorella protein. The protein digest was injected intraperitoneally 90 min before decapitation of the animal in a dose of 20 μCi/100 g body weight. The solutions were subjected to spectrophotometry on the SF-4a instrument and radioactivity was counted on an Izokap-300 counter.

EXPERIMENTAL RESULTS

The experimental data (Table 1) show that synthesis not only of total RNA, but also of total proteins was depressed in the liver of the animals in an agonal state; RNA synthesis was depressed rather more strongly.

During deep hypoxia energy-forming processes are disturbed in the tissue cells. Protein synthesis, in the modern view, is characterized by a high level of energy utilization. Consequently, an important role in the mechanisms of inhibition of protein synthesis in the liver of animals in an agonal state was evidently played by disturbance of its energy supply. The use of HBO during agony was ineffective and the animals died. Meanwhile the use of HBO ther-

apy immediately after blood loss prevented inhibition of nucleic acid and protein synthesis in the liver tissues. HBO thus prevented damage to the protein-synthesizing system in the liver cells and maintained protein synthesis at near to the control level. On the 2nd and 4th days after blood loss and a single session of HBO the general state of one-third of the animals was serious. They exhibited dyspnea and their food and defensive reflexes were drastically reduced. Of these animals 62% survived until the 4th day and 59% until the 8th day. Additional HBO (according to the scheme) increased the survival rate of the animals until the 8th day up to 70%. Comparison of the results showed that on the 4th day after blood loss RNA and protein synthesis in the liver of the animals treated with oxygen (according to the scheme) was significantly higher than in animals receiving only a single session of HBO after blood loss. The use of HBO in the recovery period after acute massive blood loss led to activation of structural metabolism in the liver, which, as we know, plays an important role in regeneration of the blood proteins. Under these circumstances the time taken for normalization of protein synthesis in the liver was shortened by HBO. Evidently the supplying of oxygen, a most important electron acceptor in the mitochondrial respiratory chain, under HBO conditions led to increased energy formation and to an increased supply of energy for protein synthesis, a process with high energy capacity, in the cells.

Thus HBO, with rational parameters, may be a highly effective factor for the prevention of irreversible changes in the tissues during increasing hypoxia, and it may also increase the intensity of structural repair processes after severe hypoxic state.

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