Metabolism in Perfused Rat Lived at Different Terms after Short-Term Hyperthermia

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The metabolic state of rat liver was studied *in vivo* 1, 6, and 18 h after single hyperthermia (42°C). It was shown that intracellular compensatory reactions involved in restoration of the energy state and realization of endogenous cytoprotective mechanisms play a role during recovery.

Key Words: *hyperthermia; liver; perfusion; metabolism*

Cells recovery after the influence of extreme environmental factors impairing structure and function of biological macromolecules is a topical problem of experimental biology. Changes in cell metabolism induced by these shifts affect the functioning of various organs and systems of the body. Effects of extreme factors on metabolic processes in organs, in particular in the liver, involved in the maintenance and correction of homeostasis are of considerable importance.

Here we studied energy metabolism in perfused rat liver at different terms after short-term whole-body hyperthermia (as an extreme proteotoxic factor).

MATERIALS AND METHODS

Experiments were performed on outbred albino rats (males and females) weighing 170-220 g. The liver was perfused *in situ* with hemoglobin-free Krebs-Henseleit bicarbonate buffer (pH 7.4) containing 5 mM glucose in a nonrecirculation system (R. Hems *et al.* [10]). The perfusate was saturated with O_2 and CO_2 mixture (95 and 5%, respectively) using a bubble oxygenator, the temperature was maintained at 37°C, and the rate of perfusion was 18-21 ml/min.

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The rats housed in individual cages were placed in a 42°C water bath for 25 min (the head was over water surface). Before this procedure, the animals were intraperitoneally injected with 0.25% droperidol in a dose of 0.1 ml/100 g body weight to avoid stress reactions. Control group rats were not subjected to hyperthermia.

Liver perfusion was conducted 1, 6, and 18 h after hyperthermia through a cannula inserted into the portal vein; the perfusate was withdrawn via the caudal vena cava cannulated after thoracotomy. The duration of liver hypoxia during cannulation did not exceed 2 min. Before surgery, the rats were intraperitoneally anesthetized with 100 mg/kg sodium thiopental. Heparin (10,000 U/kg) was injected intravenously to prevent blood coagulation during surgery. The duration of perfusion was 90 min.

The concentration of O_2 in the perfusate was measured polarographically [1], glucose was assayed by an Eksan-g conventional glucose analyzer (Lithuania), and the concentration of lactate was evaluated by a luminescent method [8,9]. The O_2 and glucose uptake and the concentrations of lactate and glucose in the perfusate were determined. The results were analyzed by Student's *t* test [4].

RESULTS

The intensity of O_2 consumption by the liver was maximum in the control, minimum 6 h after hyperthermia,

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TABLE 1. Metabolic Parameters in Rat Liver as a Function of Duration of Recovery Period (μmol/organ)

Parameter	Control	Time after hyperthermia, h		
		1	6	18
Amount of consumed O_2	773	705	537*+	756++
Glucose efflux (uptake)	913	506**	(244)*+	(158)*°
Lactate efflux	1485	2596**	2624*	1423+°

Note. *$p<0.01$ and **$p<0.05$ compared to the control; +$p<0.01$ and ++$p<0.05$ compared to previous period of observations; °$p<0.01$ and °°$p<0.05$ compared to 1 h after hyperthermia.

and intermediate 1 and 18 h after hyperthermia (Table 1). Glucose efflux was highest in the control. Glucose was detected in the perfusate also 1 h after hyperthermia, but the rate of its passage through the liver was lower, whereas 6 and 18 h after hyperthermia glucose consumption by hepatocytes prevailed (Table 1). The concentration of lactate in the perfusate was maximum 1 and 6 h after hyperthermia. In the control and 18 h after hyperthermia, the efflux of lactate was minimum (Table 1).

Decreased intensity of O_2 consumption 1 and 6 h after hyperthermia suggests dysfunction of the mitochondrial respiratory chain. These disturbances can be associated with the hyperthermia-induced intensification of lipid peroxidation in mitochondrial membranes and inactivation of respiratory enzymes [3]. ATP deficiency hinders the realization of energy-dependent cytoprotective mechanisms, including those involved in the synthesis and functioning of heat-shock proteins [5,7,11].

At the same time, reduced efflux of glucose 1 h after hyperthermia, and its intensive utilization 6 h after hyperthermia together with high lactate efflux over the first 6 h of the recovery affect to activation of glycolysis. This process improves energy supply to cells and prevents the accumulation of free radicals, which are trapped by glycolysis products [6].

The efficiency of these compensatory reactions is confirmed by activation of respiration 18 h after hyperthermia (compared to that observed 1 and 6 h after hyperthermia), which attests to increased energy potential of hepatocytes. Lactate efflux declined 18 h after hyperthermia due to high respiration rate and inhibition of glycolysis. The continuing consumption of glucose by the liver was probably related to exhaustion of glycogen stores in hepatocytes [2].

Hence, intracellular compensatory reactions involved in the recovery of the energy state of cells and realization of endogenous cytoprotective mechanisms play a role during the recovery period.

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