EFFECT OF SHORT-TERM DISTURBANCES OF THE MICROCIRCULATION ON MYOCARDIAL ENERGY METABOLISM

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Disturbance of the microcirculation by injection of high-molecular-weight dextran and vasopressin leads within a few minutes to intensification of glycolysis in the myocardium. This is shown by a lowering of the glycogen concentration, an increase in phosphorylase activity, and elevation of the pyruvate level. The concentration of high-energy phosphates still remains unchanged. Activation of glycolysis can be regarded as the initial metabolic response to hypoxia resulting from disturbance of the microcirculation.
KEY WORDS: heart; disturbance of microcirculation; glycolysis; high-energy phosphorus compounds.

Disturbance of the microcirculation as a result of changes in the rheological properties of the blood are found in many forms of pathology and, in particular, in acute myocardial infarction [2, 11]. However, the role of disturbance of the microcirculation in metabolic changes in the organs and tissues in different forms of pathology has not yet been clarified. Investigations have shown [7, 9] that a long time after experimental disturbance of the coronary circulation (by intravenous injection of high-molecular-weight dextran, which causes aggregation of red cells, combined with vasopressin, which constricts the coronary arteries) energy processes in the heart are modified. Investigation of the heart in the early stages of disturbance of the microcirculation must be of essential importance.

This paper describes the study of the concentration of high-energy phosphorus compounds and indices of glycolytic metabolism in the myocardium after short-term disturbance of the microcirculation.

EXPERIMENTAL METHOD

Experiments were carried out on chinchilla rabbits weighing 2.5-3 kg by the method described previously [6]. The ECG and respiration were recorded in all animals before and after injection of the drugs. The heart was removed 5 min after injection of vasopressin, at the time of maximal change of the ECG, and placed in a vessel containing liquid nitrogen. The frozen heart tissue was ground to powder under liquid nitrogen. Concentrations of ATP [8], ADP, AMP [1], creatine phosphate (CP) [3], inorganic phosphate (IP) [14], glycogen [15], lactic [13] and pyruvic acids [12], and phosphorylase activity [10] were determined. The results were subjected to statistical analysis [4].

EXPERIMENTAL RESULTS AND DISCUSSION

The amplitude of the T wave on the ECG was increased 2-3 min after injection of vasopressin, after preliminary administration of high-molecular-weight dextran, and it became negative after 4-5 min. Marked bradycardia and extrasystoles developed.

The concentration of high-energy phosphorus compounds was unchanged in heart tissue taken 5 min after injection of vasopressin (Table 1). However, the glycogen concentration fell by 19.4%, the pyruvic acid concentration rose by 36.9%, but the lactic acid level showed only a tendency to rise. Phosphorylase A activity was increased by 25.5% and activity of activated forms of phosphorylase, demonstrated by addition of AMP, was increased by 25.6% (Table 2).

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TABLE 1. Effect of Short-Term Disturbance of Microcirculation on Concentration of High-Energy Phosphorus Compounds (μmoles/g tissue; M ± m)

Experimental conditions	ATP	ADP	AMP	IP	CP
Control (n = 10)	7,13±0,22	0,95±0,09	0,32±0,05	9,8±0,45	3,22±0,11
Dextran + vasopressin (n = 10)	7,88±0,15	1,08±0,03	0,20±0,02	11,9±0,7	3,32±0,27

TABLE 2. Effect of Short-Term Disturbance of Microcirculation on Indices of Glycolysis (M ± m)

Experimental conditions	Control	Dextran + vasopressin	P
Glycogen, mg %	1117,2±24,9	899,3±26,2	<0,02
Lactic acid, μmoles/g tissue	4,34±0,38	4,70±0,51	
Pyruvic acid, μmoles/g tissue	0,062±0,006	0,086±0,011	<0,01
Phosphorylase A, μmoles P/g tissue/min	2,27±0,03	2,85±0,025	<0,02
Phosphorylases A + B (activation by AMP)	2,76±0,009	3,46±0,012	<0,02

The results are in agreement with data showing increased excretion of adrenalin during the first minutes of hypoxia [5, 16]. Adrenalin, through adenylate cyclase, activates phosphorylase [17] and thus is responsible for the initial stage of glycolysis.

Under the present experimental conditions the combined aggregating effect of dextran and vasoconstrictor effect of vasopressin led to disturbance of the microcirculation [6] and to some degree of hypoxia, as a result of which no decrease in the concentration of high-energy phosphorus compounds was found, for this occurs only in severe hypoxia or anoxia. Nevertheless, during the first minutes of disturbance of the microcirculation activation of glycolysis was observed in the myocardium, as shown by a fall in the glycogen level, an increase in phosphorylase activity, and an increase in the pyruvate concentration. Pyruvate, as the substrate of oxidative phosphorylation in mitochondria, provides for their more intensive function when the load on the heart is increased as the result of hypoxia.

The metabolic changes observed can be regarded as initial compensatory responses to short-term disturbances on the microcirculation.

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BIOPHYSICS OF THERMAL INJURY

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Experiments on rats showed that thermal radiation causes a much sharper increase in the subcutaneous temperature in an area of skin separated from the underlying tissues by a layer of felt than in an area of skin separated from surrounding and underlying tissues and immediately resutured in situ, or an area of intact skin. In the authors' opinion the results indicate that the blood flow does not play an essential role in the removal of heat from the skin following its exposure to radiant heat. The ability of the underlying tissues to conduct and accumulate heat is much more important.
KEY WORDS: skin; temperature regulation; thermal injury.

According to Moritz [7] the surface (critical) temperature, exposure for 8 h to which leads to total necrosis of the skin throughout its thickness, is 44°C. A similar figure is given by Fraser [3]. In the investigations of Mendelsohn and Rositter [6] and also of Henriques and Moritz [5] the difference between the surface and subcutaneous temperatures was 6-18°C. It is unnecessary to prove that this difference is due to reflection of heat by the skin surface, the cooling action of the external environment, and the absorption of heat by the various layers of the skin. The latter leads to necrosis of the cells.

Other conditions being equal, the depth of burn damage depends on the duration of thermal action and the magnitude of its deviation from the critical value given above [1, 7]. The writers' previous investigations [9] show that in the case of radiant heat, besides the above-mentioned factor, the intensity of the inflow of heat also plays an important role.

According to some workers [2-4] the degree of thermal damage to the skin depends to a definite degree on the state of the local circulation. However, Stolwijk and Hardy [10] showed that even during the first 10-15 sec, before the circulation in the skin had been disturbed by the developing necrosis, no cooling action of the blood was manifested.

With the more penetrating study of this problem the question arises of the role played by heat transmission to other parts of the body and to tissues lying under the damaged skin surface in the formation of the skin temperature. The importance of the problem, in the writers' opinion, and also according to Moserova et al. [8] is that the degree of thermal injury is affected by all factors that can reduce the skin temperature.

EXPERIMENTAL METHOD

Experiments were carried out on albino rats weighing 170-220 g (50% females and 50% males). Radiant heat was generated by a heating stove with a hole measuring 4 × 4 cm in its front wall. The temperature in the heating stove was 650°C. The temperature in the radiating aperture was monitored by a radiometric system. The power of irradiation was 1.0 W/cm^2.

The skin on the dorsal surface to be burned was depilated by means of hair clippers. Before fixation to the frame the animals were anesthetized by intraperitoneal injection of thialbarbital. The interval between the beginning of injection and irradiation in each case was 25 min. A thermistor, fixed in the midline (Fig. 1), was introduced beneath the skin of the dorsal surface, which was to be burned, from the caudal side. The readings of the thermistor were recorded every 10 sec. The scheme of the measuring system was described previously [9].

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