MYOGLOBIN CONTENT AND STATE OF THE ORGANELLES OF THE MYOCARDIUM DURING INFARCTION

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Quantitative changes in myoglobin and the subcellular organization of the myocardium were studied in the early stages of experimental cardiac infarction in dogs. Correlation was found between the myoglobin concentration and the state of the subcellular organization of the cardiomyocytes in the zone of ischemia and in the so-called intact portions of the right and left ventricles.

KEY WORDS: myoglobin; mitochondria; myofibrils; cardiomyocytes.

Myoglobin performs a respiratory function by assimilating oxygen from the blood for use in oxidative processes in muscle tissue. In some species of animals the myoglobin content is different in heart muscle [1]. The distribution of myoglobin also differs quantitatively in different parts of the heart [7, 13].

Histochemical methods of investigation have revealed [4] that myoglobin in the cardiomyocyte is located at the level of the A disk of the myofibrils, in skeletal muscles it lies on both sides of the Z bands, and in smooth-muscle cells it occurs as chains lying along the muscle cell. This localization of myoglobin in the muscle cell corresponds to the arrangement of the mitochondria in it.

In the investigation described below a parallel study was made of quantitative changes in myoglobin and the subcellular organization of the myocardium in the same parts of the heart in the early stages of disturbance of the coronary circulation.

EXPERIMENTAL METHOD

Experiments were carried out on 22 mongrel dogs weighing 18-25 kg. In 17 dogs the blood supply to the myocardium was disturbed by ligation of the anterior descending branch of the left coronary artery at the boundary between its upper and middle thirds. The ECG was recorded in every case. The animals were killed 2-3 and 24 h after ligation of the coronary artery. To investigate the myoglobin weighed samples of myocardium were taken from the anterior wall of the left ventricle 2-3 cm distally to the site of the ligature and also from the so-called intact parts of the myocardium: from the right ventricle and from the posterior wall of the left ventricle. These parts of the heart were subjected to pathological and electron-microscopic investigation. Similar investigations were carried out on five healthy dogs which acted as the control. The myoglobin concentration was determined spectrophotometrically [14]. All the tests were repeated. Sections were cut on the LKB-8800 ultratome and examined in the JEM-7A electron microscope with an accelerating voltage of 80 kV.

EXPERIMENTAL RESULTS

Changes in the myoglobin content in the early stages after disturbance of the coronary blood supply in the different parts of the heart are given in Table 1.

*Deceased.

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TABLE 1. Changes in Myoglobin Content (mg/g tissue) in Different Parts of Heart in Stages of Ischemia and Formation of Experimental Myocardial Infarcts in Dogs (M ± m)

Time after ligation of coronary artery	Anterior wall of left ventricle	Posterior wall of left ventricle	Right ventricle
Control	4,66±0,31	4,60±0,25	3,73±0,14
2-3 h	3,11±0,16	4,52±0,54	3,37±0,4
24 h	2,79±0,105	3,72±0,52	6,22±0,74

Within 2 to 3 h after ligation of the coronary artery the myoglobin content in the zone of ischemia was reduced. The myoglobin content in the posterior wall of the left ventricle and in the right ventricle was virtually unchanged. A further decrease in the myoglobin content in the zone of ischemia was observed 24 h after production of the experimental myocardial infarct. At the same time there was a small decrease in its content in the posterior wall of the left ventricle. The opposite effect was observed in the myocardium of the right ventricle: Its myoglobin content at this time was sharply increased. A parallel study of the ultrastructural organization of the myocardium showed the presence of intercellular and intracellular edema, swelling of the mitochondria, partial destruction of their cristae, and translucency of their matrix in the zone of ischemia 2-3 h after ligation of the coronary artery. Fragments of the inner membranes accumulated in the translucent matrix of many of the mitochondria. Fragments of individual cell organelles, including mitochondria, were found in the intercellular space adjacent to cardiomyocytes with disintegrated sarcolemma. The myofibrils in most cardiomyocytes were in an uncontracted state and large I disks and H zones were obsrved in them. Meanwhile, in the muscle fibers of the posterior wall of the left ventricle swelling of the mitochondria also was observed, although this was not as severe as in the zone of ischemia. Disorganization of the cristae was observed in the mitochondria, but no marked destruction of the cristae had taken place. The myofibrils were in a contracted state. In the right ventricle changes in the ultrastructural organization of the myocardium were less marked: 2-3 h after disturbance of the coronary circulation vacuolation of individual mitochondria was observed and, in some muscle fibers, the myofibrils were overcontracted with the formation of contraction poles in them. The degree of the destructive changes in the myocardium was much greater 24 h after ligation of the coronary artery. In the zone of ischemia in some cardiomyocytes most of the mitochondria were destroyed. The mitochondria were swollen, their cristae were completely destroyed, and the outer mitochondrial membrane appeared to consist of only a single layer. The myofibrils were fragmented at the boundaries of their A and I disks. In the posterior wall of the left ventricle at the same period considerable swelling of the mitochondria with disorganization and destruction of the cristae were observed. Many myofibrils were in an uncontracted state. In some cardiomyocytes of the right ventricle hyperplasia of the mitochondria was observed but, as a rule, the ultrastructural organization of the myofibrils was unchanged (Figs. 1-3).

The myoglobin content in the muscle is known to be an indicator of the intensity of oxidative processes. The higher the myoglobin content in a muscle, the more able it is to accumulate oxygen and to intensify its respiratory metabolism. The oxygen reserve bound with myoglobin is important in local disturbances of the circulation and in anoxia of varied etiology. A matter of definite importance for clinical practice is the study of the quantitative distribution of myoglobin in the heart muscle during myocardial infarction. Investigations have shown that the necrotic changes developing in muscles following a disturbance of their blood supply lead to a reduction in their myoglobin content. Biochemical methods have revealed a decrease in the myoglobin concentration in the infarcted zone of the myocardium [2, 6]. Spectrophotometric investigations have revealed myoglobin in the blood serum and urine of patients with myocardial infarction, its concentration being highest in the first days of the disease [12]. Cases of severe infarction with excretion of a brown urine during the first 2-3 days [9], due to myoglobinuria, have been described. It has been shown [3] that the myoglobinuria in patients with myocardial infarction is based on the circulation of degenerated cardiomyocytes in the blood stream. Fragments of cardiomyocytes discovered electron microscopically in the intercellular space in the present investigation confirm this hypothesis.

The present experiments showed a decrease in the myoglobin content in the infarcted region of the myocardium compared with its "intact" zones. The decrease in the myoglobin content in the posterior wall of the left ventricle 24 h after ligation of the coronary artery, with a simultaneous increase in its content in

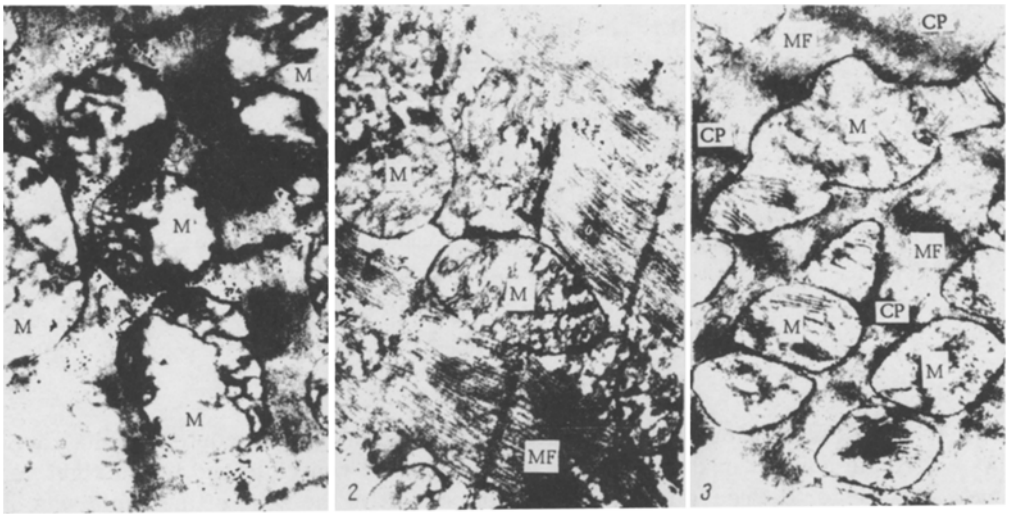

Fig. 1 Fig. 2 Fig. 3

Fig. 1. Cardiomyocyte of anterior wall of left ventricle. Greatly swollen mitochondrion (M) can be seen, with its cristae completely destroyed, and the outer membrane in some areas appearing to consist of only one layer; 24 h after ligation of coronary artery, 25,000×.

Fig. 2. Cardiomyocyte of posterior wall of left ventricle. Mitochondria (M) swollen, their cristae disorientated, their matrix translucent, myofibrils (MF) in an uncontracted state, large I disks visible; 24 h after ligation of coronary artery, 40,000×.

Fig. 3. Cardiomyocyte of right ventricle. Among intact myofibrils (MF) many mitochondria (M) have accumulated; 24 h after ligation of coronary artery, 20,000×.

the right ventricle is evidence that the heart reacts to a local disturbance of its blood supply as a single entity. Acute ischemia in the region of the anterior wall of the left ventricle was accompanied by a response not only of the left, but also of the right zones of the heart. However, whereas in the left ventricle (its posterior wall) the changes were consistent in direction with those in the zone of ischemia and differed only in their severity, in the right ventricle there was a marked increase in the myoglobin content. It can tentatively be suggested that the increase in the myoglobin concentration in the right ventricle was aimed at maintaining its increased activity as a result of the functional insufficiency of the left ventricle. The results are in agreement with the existing view that the right ventricle is more adaptable than the left to changing demands under pathological conditions, as is supported by morphological [5] and biochemical [8, 10] investigations which have demonstrated considerable hyperfunction of the energy-forming systems of the right ventricle and a higher content of reserve energy substrates in it.

As has already been stated, attempts have been made to show correlation between the myoglobin content and the state of the mitochondria [4, 11]. In this investigation correlation was found between the myoglobin content in the heart muscle in the early stages of experimental cardiac infarction and the subcellular organization of the heart, including changes in the mitochondria.

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EFFECT OF THE ASSISTED CIRCULATION ON MYOCARDIAL ULTRASTRUCTURE

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The effect of a method of assisted circulation (counterpulsation) on the ultrastructure of the myocardium was studied in dogs. Electron microscopy revealed a sharp increase in the glycogen content in the heart muscle cells, mitochondria with a highly osmophilic, finely granular matrix, and high pinocytotic activity of the capillary endothelial cells. The results are evidence of metabolic changes in the myocardium and, in particular, that the myocardial muscle cells are functioning at a lower energy level. The changes discovered in the myocardial ultrastructure evidently account for the beneficial therapeutic effect of the method.

KEY WORDS: assisted circulation; myocardial metabolism; glycogen; mitochondria.

Despite many investigations of the assisted circulation, the true character of the processes taking place under these circumstances in the body is still far from completely understood [3, 7, 10].

The object of this investigation was to study the effect of the assisted circulation, using the counterpulsation method, on the ultrastructure of the myocardium in intact animals.

EXPERIMENTAL METHOD

Seven dogs weighing 15-25 kg were used. Under endotracheal anesthesia (morphine, thiopental sodium, listhenon) the thorax was opened in layers in the third-fourth intercostal spaces on the left side and the subclavian artery was isolated. A cannula, connected to the output tube of a valveless blood pump, with a common inlet and outlet for the blood, was introduced into the lumen of the artery. The pump was connected to a pneumatic drive mechanism and cardiosynchronizer. The ECG and the pressure in the ascending aorta were recorded during the experiments, the acid–base balance and the free hemoglobin concentration in the blood plasma were determined, the "time-tension index" (TTI) and the external work of the left ventricle were calculated.

After the initial parameters of the hemodynamics had been measured and blood samples taken, the pneumatic drive mechanism was switched on and the assisted circulation commenced under counterpulsation conditions as described previously [3, 13].

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