ACTIVITY OF CERTAIN ENZYMES OF THE SERUM AND HEART MUSCLE IN NORMAL CONDITIONS AND IN MYOCARDIAL LESIONS OF NEUROGENIC NATURE

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Myocardial infarction, both clinically and experimentally, is accompanied by changes in the activity of certain enzyme systems of the blood serum and heart muscle. An increase in the activity of the transaminases, aldolase, lactate dehydrogenase (LDH), and creatine kinase in the blood serum and a decrease in their activity in the focus of necrosis are observed in infarcts of the myocardium caused by ligation of the coronary artery [5, 6, 15, 16]. Results have also been obtained indicating changes in enzymes in necroses of the myocardium caused by injection of isoproterenol and other chemical substances [7, 20].

One of the authors (E.A.B.) has previously shown that potassium chloride, when injected into the lateral ventricles of the brain, causes activation of the sympathico-adrenal system, resulting in the development of focal injuries to the myocardium in the form of micronecroses and cloudy swelling [2].

It was important to determine the biochemical characteristics of the new models of experimental myocardial necrosis caused by injection of potassium chloride into the lateral ventricles of cats.

In the present investigation studies were made of the enzymes aspartate ketoglutarate transaminase (AKT), LDH, and phosphocreatine transferase (PCT), the changes in which are most characteristic of myocardial infarcts of different etiology.

EXPERIMENTAL METHOD

Experiments were carried out on cats. Potassium chloride (0.5 ml of a 0.25 M solution) was injected into the lateral ventricles by means of a stainless steel cannula-conductor [9, 13].

In a separate series of experiments the enzymes were investigated after 2 injections of potassium chloride at an interval of 24 h. In all the experimental animals the electrocardiogram (ECG) was taken in 3 standard leads.

Blood was obtained from the femoral vein of the animals.

The heart was extracted under Nembutal anesthesia, perfused for 45 sec with cold 0.15 M KCl solution, and minced on ice. A homogenate was prepared in 0.05 M phosphate buffer (pH 7.4, 1:10) for estimation of AKT and in 0.1 M phosphate buffer (the same pH 1:6) for estimation of LDH. The PCT was determined in extracts prepared in 0.9% NaCl solution, after standing for 24 h in the cold. The AKT activity was determined by Umbreit's method as modified by Paskhina [4, 18] and expressed in micrograms of sodium pyruvate. The LDH was estimated from the reaction of enzymic reduction of pyruvate into lactate in the presence of $NADH_2$ [19]. The unit of activity was taken to be a decrease in optical density of 0.001 at 340 mμ in 1 min. The PCT activity was estimated from the formation of creatine from creatine phosphate in the presence of molybdate [1, 8] and it was expressed in micrograms of creatine.

RESULTS AND DISCUSSION

Injection of potassium chloride into the lateral ventricles was accompanied by changes in the content of AKT and LDH in the blood serum. The AKT activity 3 h after injection of potassium chloride showed a clear increase – to 51± 12 units (normal value 21± 1.6 units). This increase became maximal after 24 h (71± 13.5). After 48 h the

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Activity of AKT, LDH, and PCT in the Heart Muscle in Normal Conditions and after Injection of Potassium Chloride, in Units of Activity/g Tissue

	AKT	LDH	PCT
Normal conditions	104 000±2 400	276 700±17 000	1 090±90
After injection of KCl	100 000±5 000	293 000±18 000	940±100

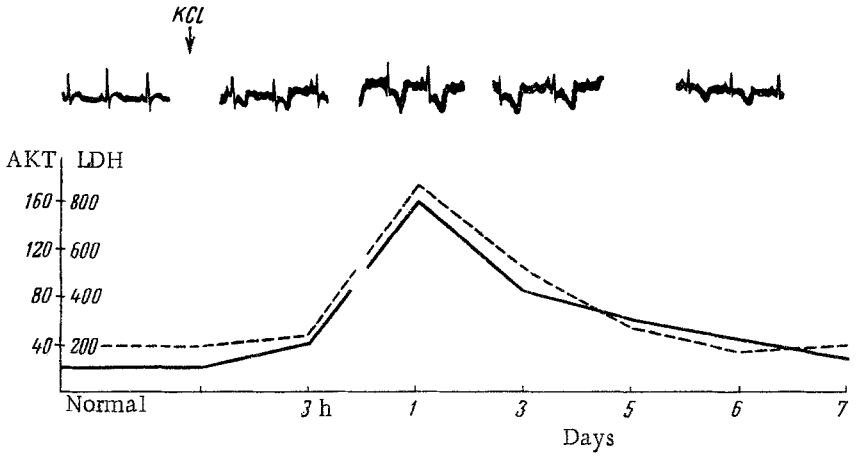

Fig. 1. Changes in the ECG and activity of aspartate-ketoglutarate transaminase (AKT) (continuous line) and lactate dehydrogenase (LDH) (broken line) in the blood serum of a cat at various times after injection of potassium chloride (results of one experiment). Along the axis of abscissas—activity (in units); along the axis of ordinates—time (in hours and days).

content of AKT fell gradually, and was normal after 6-7 days. At the same time the LDH content rose considerably, to reach 285±32 units after 3 h; it remained high for 24 h and returned to normal on the second day.

In all the experiments injection of potassium chloride caused prolonged changes in the ECG characteristic of myocardial ischemia: inversion of the T wave and the appearance of a discordant T wave in leads I and III, and a deep Q wave.

In most experiments, the increase in the levels of AKT and LDH corresponded to disturbances in the ECG, and these in turn reflected the degree of myocardial injury (Fig. 1).

A second injection of potassium chloride leading, judging by the ECG and the results of morphological investigations, to an increase in the size of the necrotic foci in the myocardium, caused a still greater increase in the activity of AKT and LDH (Fig. 2).

After intraventricular injection of potassium chloride, the appearance of PCT in the serum 24 h after injection was observed only in 3 experiments, reaching 50-60 units. As a rule no PCT was present in the serum of the healthy animals. Characteristically the increase in the PCT content was accompanied by a considerable rise in the levels of AKT and LDH and by sharp changes in the ECG.

It is clear from the table that no significant differences were found in the content of the investigated enzymes in the heart muscle tissue in normal conditions and after injection of potassium chloride.

The results of these experiments showed that in the presence of micronecroses of the myocardium caused by injection of potassium chloride into the lateral ventricles of the brain, the activity of AKT and LDH in the blood serum was increased.

On the basis of the correlation between the degree of injury to the myocardium and the increase in activity of the serum enzymes, it may be assumed that this increased activity of the serum enzymes was due to loss of enzymes from the necrotic areas of the myocardium as a result of an increase in the permeability of the cell membranes [14, 17].

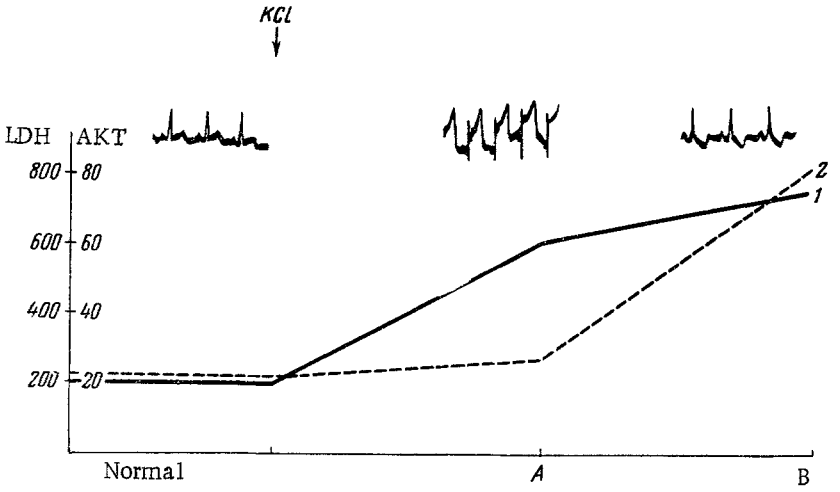

Fig. 2. Changes in the ECG and activity of aspartate-ketoglutarate transaminase (AKT) (1) and lactate dehydrogenase (LDH) (2) in the blood serum of a cat after a single (A) and repeated (B) injection of potassium chloride (results of one experiment).

The absence of changes in the PCT activity in most experiments demonstrates that, by comparison with AKT and LDH, PCT is evidently a less sensitive index of the presence of micronecroses of the myocardium.

Because of the diffuse character of the micronecroses, it was impossible to investigate the activity of the enzymes separately in healthy and necrotic areas of the myocardium. This may have been the reason why no changes were found in the contents of the enzymes in the heart muscle. The absence of visible changes in the activity of the enzyme systems may also be due to a compensatory increase in the enzyme activity in unaffected areas of the myocardium. Such a compensatory increase in the activity of several enzymes has been found in myocardial infarcts caused by ligation of the coronary artery [3, 11].

However, the problem of the mechanism of the increased blood enzyme activity after intraventricular injection of potassium chloride can be finally solved only after the discovery of an increase in the activity of enzymes specific for the heart in the blood serum. Experimental investigations in this direction are proceeding.

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