

PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

SERUM ALDOLASE CONTENT OF THE BLOOD OF DOGS WITH EXPERIMENTAL (MYOCARDIAL) INFARCTION

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In recent years, the most actively pursued field of medical research has been that dealing with the problems of acute coronary insufficiency and of myocardial infarction. It appeared from the discussions held at the XIV Congress of Therapists that, despite the considerable advances achieved in the study of myocardial infarction, many aspects of the problem still await solution. Among these is the study of biochemical changes taking place in the myocardium during the course of this disease.

Recently published papers on myocardial infarction have drawn attention to the importance of changes in the myocardial enzyme systems, and in particular to the transaminases, which are responsible for transamination reactions. These researches have led to the provision of a new diagnostic method, permitting the assessment of the activity of the necrobiotic process [1, 5, 6].

It is known that considerable disturbances of the carbohydrate metabolism of the myocardium are encountered during infarction, glycolysis being affected in particular. There can be no doubt that the enzyme systems taking part in this process must undergo some changes. We have undertaken a special study of one of the enzymes concerned in glycolysis, viz., aldolase.

We have been unable to trace any Soviet work on changes in aldolase activity in myocardial infarction; only quite recently have we found any references to changes associated with acute coronary insufficiency in the foreign literature [7]. Since we considered that this question has been insufficiently elucidated, we undertook an investigation into changes in aldolase content in myocardial infarction, and into the possibility of applying our findings for diagnostic and prognostic purposes.

O. Meyerhof and K. Lohmann [8], in 1934, discovered a glycolytic enzyme, which they named zymohexase, responsible for catalyzing the breakdown of fructose 1:6-diphosphate into two triose phosphate molecules (one molecule of glyceraldehyde 3-phosphate and one molecule of dihydroxyacetone phosphate). This enzyme was later called aldolase.

In 1943 O. Warburg and W. Christian [9] were able to isolate this enzyme from tissues, in a crystalline form, and to establish the importance of its role in tissue glycolytic processes.

Subsequent papers have shown that changes in the content of this enzyme in the blood serum and tissues are encountered in various conditions involving tissue destruction and necrosis, such as tumors [9], liver disease [10], and viral diseases [4]. The highest aldolase contents are found in skeletal muscle, heart muscle, and liver [11], for which reason the widest variations in its content were found in diseases of these tissues.

It is noteworthy that in severe myodystrophic conditions there is a pronounced fall in muscle aldolase content, with a simultaneous rise in serum aldolase [5].

In view of the above considerations raised levels of serum aldolase might be expected to occur in

myocardial infarction, involving marked necrotic and dystrophic changes in the myocardium. Since the rise in serum aldolase content is associated with its liberation from injured cells, there should be a certain correlation between the degree of myocardial infarction and the rise in serum aldolase. These were the problems which we hoped to clarify in our research. Our investigations were performed on both experimental clinical material.

The present communication deals only with the experimental part of our studies, on the aldolase content of blood serum at various times after induction of myocardial infarction in dogs.

EXPERIMENTAL METHODS

Myocardial infarction was induced by ligation of the left coronary artery of dogs. This operation leads to the appearance of severe necrotic lesions of the anterior wall of the left ventricle, in the interventricular septum, and at the apex of the heart [2].

We ligated the left coronary artery of 16 dogs, of which two died within 20-25 minutes of ligation. Serum aldolase levels were determined for the surviving 14 dogs, at various times after the operation. Since the operation itself was associated with considerable skeletal muscle trauma, and with possible liberation of aldolase therefrom, we also determined the serum aldolase of 5 dogs which had been subjected to thoracotomy alone, without coronary ligation.

Electrocardiographic examination of all the operated dogs gave evidence of changes characteristic of myocardial infarct: negative T_1 and T_2 waves, displacement of the RS-T interval, accentuated Q wave. Autopsy of 3 dogs which died some time after ligation showed profound necrotic changes in the anterior wall of the left ventricle.

Aldolase was determined by the method of Dounce and Thannhauser, as described by V. I. Tovarnitskii and E. N. Valuiskaia.

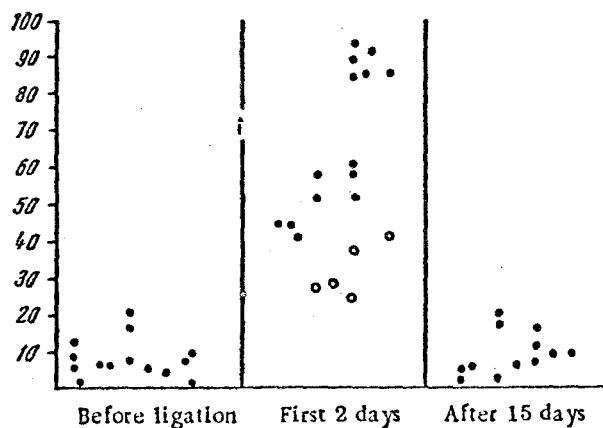


Fig. 1. Serum aldolase content of a dog subjected to experimental infarction and thoracotomy.

Aldolase was determined before ligation of the coronary artery, during the first 2 days after ligation, and then at intervals up to the 20th day.

A marked rise in serum aldolase was observed during the first 2 days after operation (Fig. 1). The aldolase content was in many cases 8-9 times higher than the initial level. In the control group (thoracotomy not followed by ligation) the rise in serum aldolase was much smaller, amounting to $2\frac{1}{2}$ to 4 times the initial level (represented by circles in Fig. 1).

We also observed a correlation between the size of the myocardial infarct and the rise in serum aldolase content.

Our findings are exemplified by 2 dogs, which died in a late stage of myocardial infarction. The postoperational condition of one dog was very grave, with severe symptoms of cardiac insufficiency, and with considerable electrocardiographic changes. Serum aldolase was 9 times higher than normal on the second day after the operation. The dog died on the 8th day. Autopsy revealed extensive infarction of the anterior wall of the left ventricle and of the apex and septum (Fig. 2). In the second dog, which died 21 days after ligation of the coronary artery, the myocardial infarction was much smaller, and was restricted to the anterior wall of the left ventricle (Fig. 3). The rise in serum aldolase was much smaller in this case (up to 58).



Fig. 2. Experimental myocardial infarction (↑) after high ligation of the left coronary artery.

finding points to the possible diagnostic value of blood aldolase determinations in cases of suspected myocardial infarction.

These examples reveal a certain proportionality between the extent of the necrotic lesions of the heart wall and the level of serum aldolase. This finding can doubtless be applied for clinical purposes, both for diagnosis and prognosis.

In all the 14 cases observed by us we found a close correlation between the extent of the necrobiotic changes in the heart muscle and the increase in blood aldolase content.

In a number of experiments we compared the times of appearance of the biochemical changes in the blood after ligation of the coronary artery with those found after simple thoracotomy (control experiments).

We found the same rise in serum aldolase during the first few hours after ligation as after control thoracotomy, and this rise can most probably be ascribed to trauma of skeletal muscles associated with the operation. However, the aldolase content continued to rise 5 hours after ligation, and attained considerable proportions after 18 hours. Electrocardiograms taken at this stage did not always show the characteristic signs of myocardial infarction. This

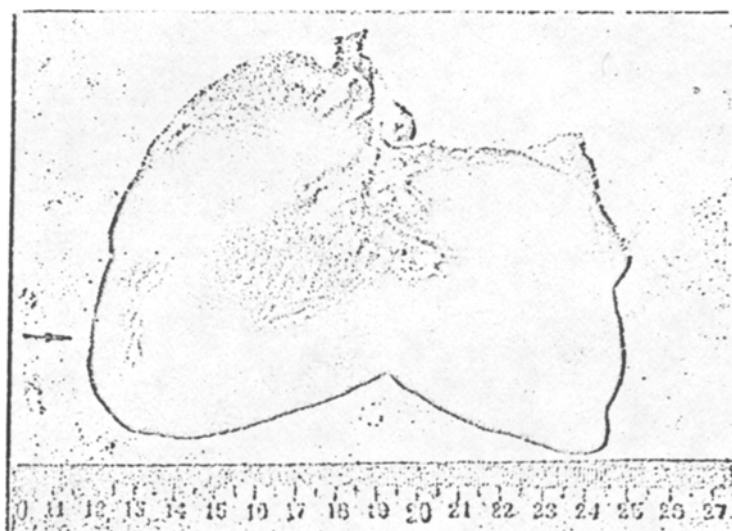


Fig. 3. Experimental myocardial infarction (→) after low ligation of the left coronary artery.

Blood aldolase levels began to fall on the 3rd-4th day, and were normal after the 15th day.

We determined blood aldolase in a series of 12 patients suffering from myocardial infarction, and in a series of 15 patients with "spurious" infarction, in whom the diagnosis of coronary thrombosis had been rejected on clinical grounds; our findings resembled those reported above for experimental animals.

SUMMARY

The content of aldolase in the blood serum was examined in dogs with experimental infarction induced by ligation of the left coronary artery. It was established that the content of aldolase is increased in these dogs by 4-5 times in comparison with that in the control animals. The concentration of the enzyme begins to increase 5-6 hours after the ligation of the coronary artery and reaches its maximum within the first 2 days. By the 15th day the content of aldolase returns to the normal level. The increase of aldolase concentration depends on the severity of myocardial infarction. Determination of the concentration of aldolase in the blood serum may be used for clinical diagnosis in suspected myocardial infarction.

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