ATP-ASE ACTIVITY OF MYOCARDIAL EXTRACTS FROM RABBITS WITH ALLOXAN DIABETES

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The ATP-ase activity in the myocardium is reduced in rabbits with alloxan diabetes. Injection of insulin restores it to normal.

Experiments have shown that phosphorylation of creatine phosphate in myocardial homogenates of rats with alloxan diabetes is sharply reduced if succinate and malate are used as oxidation substrates [10]. The writer's previous investigations [3] showed, however, that the content of high-energy phosphorous compounds in the myocardium of rabbits with alloxan diabetes is not reduced. These findings are in full agreement with those in the literature [11]. Goranson and co-workers [9] found that the increase in P^{32} incorporation into ATP under the influence of insulin is not accompanied by an increase in ATP content. It has also been shown [6, 7] that the ATP content is not substantially changed under the influence of insulin, but that dephosphorylation of ATP is intensified [5]. It has accordingly been concluded that the utilization of high-energy phosphorous compounds in simultaneously stimulated by insulin. The normal content of high-energy phosphorous compounds in the heart muscle in diabetes, despite the diminished generation of high-energy phosphorous compounds during phosphorylation of creatine phosphate under these conditions, is most probably due to a decrease in their utilization.

Most of the loss of ATP during myocardial contraction is known to take place during the conversion of the potential energy of ATP into the kinetic energy of muscular contraction during its interaction with actomyosin. The velocity of this reaction depends on ATP-ase activity and the quantity of contractile protein (actomyosin). The writer's previous investigations showed a decrease in protein synthesis in the myocardium of rabbits with alloxan diabetes [3], and this could be one of the factors limiting this reaction. In addition, according to data in the literature [1, 2, 4], ATP-ase activity is reduced in the kidneys, liver, brain, and especially, in the muscles of diabetic animals, and also that the activity of this enzyme is increased if diabetic animals are treated with insulin [1, 2].

The object of this investigation was to study the ATP-ase activity of extracts of the myocardium of rabbits with alloxan diabetes.

EXPERIMENTAL

Experiments were carried out on 21 rabbits: 13 animals with alloxan diabetes of one month's duration and eight controls. Six of the 13 rabbits with alloxan diabetes received injections of insulin. Alloxan diabetes was produced by intravenous injection of a 5% solution of alloxan in a dose of 130-150 mg/kg body weight. The blood sugar was determined by the Hagedorn–Jensen method. Insulin (insulin-zinc suspension) was injected daily throughout the period of diabetes in a dose of 2 units/kg body weight. The same dose of long-acting insulin was injected into the animals 1.5 h before their sacrifice. The ATP-ase activity was determined by the method of Bonting and co-workers [8]. The sodium salt of ATP (acid) (Reanal) was used

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as substrate. The composition of the incubation mixture was as follows (in μmoles): ATP 0.1, tris 92, Mg^{++} 1, K^{+} 5, Na^{+} 58. The ATP-ase activity of the myocardial extracts of the rabbits was determined from the increased in inorganic phosphorous after hydrolysis of ATP in the course of incubation for 20 min at 37°, and it was expressed in μmoles phosphorus (P_i) per gram fresh weight of tissue.

EXPERIMENTAL RESULTS

The ATP-ase activity of myocardial extracts from the control animals averaged 4.5 ±0.12 μmoles P_i/g fresh weight of tissue after incubation for 20 min.

In rabbits with alloxan diabetes of one month's duration a marked decrease in the ATP-ase activity of the myocardial extracts was observed, as shown by a decrease in the formation of inorganic phosphorous during enzymic hydrolysis of ATP to 3.6 ± 0.1 μ moles P_i/g fresh tissue, or a decrease of 20% relative to the control ($P < 0.001$). Prolonged administration of insulin to rabbits with alloxan diabetes helped to restore the ATP-ase activity of the myocardial extracts, to reach a mean level of 4.3 ±0.12 μmoles P_i/g fresh weight of tissue ($P < 0.001$).

In rabbits with alloxan diabetes, because of the decrease in ATP-ase activity in the myocardium, and also because of the slowing of protein synthesis in the myocardium observed by the writer previously [3], the utilization of ATP during contraction of the myocardium is thus disturbed. As a result, the content of high-energy phosphorous compounds remains unchanged, despite their reduced formation in the myocardium in diabetes.

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