INTENSITY OF GLYCOGEN RENEWAL IN THE MYOCARDIUM OF RABBITS WITH ALLOXAN DIABETES

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UDC 616.379-008.64-092.9-07:616.127-008.934.586.3-074

Despite an increase in the glycogen content in the myocardium of rabbits with alloxan diabetes, the intensity of glucose-C^{14} incorporation into the glycogen of their myocardium is sharply reduced. Injection of insulin into rabbits with alloxan diabetes helps to restore the normal intensity of glucose incorporation into myocardial glycogen.

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Cold [6] and Fisher [9] consider that myocardial degeneration in diabetes mellitus is caused by inadequate glucose utilization and depression of glycogen synthesis in the myocardium.

Nevertheless, other investigations [1, 2, 7] have shown that the glycogen content in the myocardium of animals with experimental diabetes is increased. As a result of the work of Morgan [11] and Park [12], who demonstrated the effect of insulin on permeability of cell membranes by facilitating the utilization of glucose, it is evidently impossible to explain the accumulation of glycogen in the myocardium without the use of isotope indicators to investigate glycogen renewal. Cavert and co-workers [5] perfused the isolated heart and showed that the further a compound is from the beginning of the glycolytic pathway, the slower its rate of incorporation into glycogen. The most promising line of attack is by studying the renewal of glycogen in the myocardium after administration of its precursor—glycose-C^{14}. Prokhorova and co-workers [3] established a relationship between the rate of incorporation of glucose-C^{14} into the brain and liver of rats and the glycogen content in the tissues of these organs: the higher the glycogen content in the organ, the less isotope was incorporated. Feller and co-workers [8] studied the circulation of glycose-C^{14} in depancreatized dogs and found a decrease in the content of glucose-C^{14} in the heart. A negative glucose balance in the myocardium of depancreatized dogs was observed by Himvich and Goldfarb [10].

The object of the present investigation was to study the glycogen content in the myocardium and the intensity of its renewal in rabbits with alloxan diabetes and after injection of insulin in vivo with the aid of glucose-C^{14}.

EXPERIMENTAL METHOD

To study the intensity of glycogen metabolism, glucose-C^{14} ($NaHC^{14}O_3$) was injected into rabbits weighing 3-3.5 kg after fasting for 18 h in a dose of 6000-8000 pulses/kg body weight [4]. The animals were sacrificed 1 h later, and glycogen extracted from the myocardium by Pflüger's method with triple reprecipitation. The glycogen residue thus obtained was dissolved in 1 ml hot water, transferred carefully to a metal target, and dried; its radioactivity was then determined. After measuring of the radioactivity, the quantity of glycogen in the residue was determined (after hydrolysis of the glycogen). The glucose content was determined by the Hagedorn Jensen method. The total radioactivity (content of total C^{14}) in the heart muscle homogenate was also investigated.

Calculations.

1) Relative radioactivity of glycogen = pulses/min/mg glycogen.

2) Percentage of incorporation of C^{14} into glycogen $= \frac{\text{activity of glycogen/g myocardium}}{\text{activity injected per gram body weight}} \cdot 100.$

Laboratory of Pathological Physiology, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician of the AMN SSSR N. A. Fedorov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 4, pp. 54-55, April, 1969. Original article submitted July 24, 1968.

3) Percentage of incorporation of C^{14} into homogenate $= \frac{\text{activity of homogenate per gram myocardium}}{\text{activity injected per gram body weight}} \cdot 100.$

Alloxan diabetes was produced by intravenous of alloxan into the rabbits (130 mg/kg body weight). Insulin (IZS) was injected subcutaneously in a daily dose of 2 units/kg body weight. An injection of insulin with ordinary action in a dose of 2 units/kg body weight was given to the animals 1.5 h before sacrifice.

EXPERIMENTAL RESULTS

The total myocardial radioactivity (carbon incorporated into various compounds expressed as percentages of incorporation of radioactivity of homogenates of 1 g heart muscle) of rabbits with alloxan diabetes differed very little from that of control animals (control 7.4%, diabetes 5.7%). The absolute content of glycogen in the myocardium of rabbits with alloxan diabetes was increased (control 0.55 g%, diabetes 0.72 g%). However, despite this, the relative radioactivity of glycogen in the myocardium was sharply reduced (75 ± 10 and 7.8 ± 2 pulses/min/mg glycogen; $P < 0.001$), only 10.4% of the control level.

Prolonged administration of insulin to rabbits with alloxan diabetes stimulated the intensity of incorporation of glucose-C^{14} into glycogen (without insulin 7.8 ± 2, with administration of insulin 50.7 ± 3.29 pulses/min/mg glycogen; $P < 0.001$) also indicates marked inhibition of this process in the myocardium of rabbits with alloxan diabetes.

Injection of insulin into animals facilitates restoration of disturbed glycogen synthesis from glucose-C^{14} to normal (control 6.1%, animals with diabetes receiving insulin 6.9% per gram tissue).

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