Transmural gradients in myocardial metabolic rate

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Summary

To examine the 2-deoxyglucose (2-DG)-method for myocardial tissue, glucose uptake was measured directly and via the 2-DG-technique in 16 isolated perfused guinea pig hearts. A correlation ($r = 0.7; p < 0.01$) between both methods was found. In the in situ working canine heart 2-DG revealed a 20% higher glucose uptake of the subendocardial layers as compared with the subepicardial. Blood flow to these layers, estimated by albumin aggregates, exceeded that to the subepicardial by 82%. Thoracotomy resulted in a homogeneous distribution of blood flow and tissue PO$_2$, comparable to a homogeneous distribution of glucose uptake in isolated perfused hearts.

A nonuniform distribution of myocardial blood flow has been demonstrated in tracer particle studies. Depending on particles properties and size, subendocardial flow exceeded subepicardial by 10 to 80% (1, 2). These inhomogeneities have not only been attributed to methodological problems but also to inhomogeneities in myocardial metabolism.

In 1977 Sokoloff and collaborators (3) developed a method to determine regional glucose consumption of brain tissue, using 2-deoxyglucose (2-DG) uptake as an indicator. We tried to adapt this method to determine regional myocardial metabolic rate of glucose. Preliminary results have already been published (4, 5).

This study was designed
1. to validate the 2-DG-method for myocardial tissue by answering the question whether there is a correlation between myocardial D-glucose consumption and a consumption calculated via the 2-DG-method,
2. to determine regional myocardial glucose consumption in the in situ working heart, and
3. to determine the influences of the experimental conditions on regional glucose consumption.

The results were compared with those of blood flow and tissue PO$_2$ obtained in former experiments.

Method

1) In 16 isolated guinea pig hearts, performing no external work, 60 minutes perfused by Govier's solution, containing D-glucose, 2-DG and Insulin, D-glucose uptake was determined by measuring the glucose extraction from the perfusion

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solution with and without β-adrenergic stimulation. At the end of the experiment 14C-DG and DG-6P content (Q-2-DG) of the tissue was measured by a liquid scintillation method and glucose uptake (Q, mg/100 g x min) was calculated by the following formula:

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Q = \frac{Q - 2-DG \times 100}{\text{min} \times \text{sample weight}} \times \frac{[\text{Glucose}]}{[\text{DG}]}
\]

where [Glucose]/[DG] is the ratio of the respective concentrations in the perfusion solution throughout the experiment.

2) Regional myocardial glucose consumption in the in situ working heart was determined in 8 anesthetized dogs (MABP 109 ± 7 mmHg, PaO₂ 92 ± 14 mmHg). 14C-2-DG (10 μCi/kg) was injected intravenously. The ratio of the arterial D-glucose and 2-DG concentrations was measured throughout the experiment (60 min). At the end of the experiment the animals were sacrificed, the heart was quickly removed, divided into three parts and frozen in -70 °C isopentane.

From these pieces, samples (0.2 g) from the subepicardial, middle and subendocardial layer of the basal, middle and apical parts were taken. 14C content of the samples was again determined by liquid scintillation techniques. D-glucose consumption was calculated as described above.

Fig. 1. Relation between D-glucose consumption determined by direct extraction measurement and by the 2-Deoxyglucose method. Isolated perfused guinea pig heart (n = 16).