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Flux Of Glucose Through Pentose Phosphate Pathway And Glycolysis In Mouse Hearts Subjected To Low-Flow Ischemia

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Abstract

Introduction

The molecular events that lead to irreversible myocardial damage during severe ischemia remain poorly understood. Changes in cytosolic redox status and ability of mitochondria to oxidatively metabolize fatty acids and carbohydrates have been implicated in ischemic Injury. The pentose phosphate pathway (PPP) produces NADPH, which can be used to maintain glutathione in its reduced state, providing protection against oxidative damage. The rate of glycolysis during ischemia determines extent of ischemic injury. We investigated flux of glucose through PPP and glycolysis in mouse hearts subjected to low-flow ischemia in this study.

Methods

Isolated mouse hearts were perfused in Langendorff mode with 10mM [1,2-$^{13}C_2$]-glucose for 60min, followed by 90min low-flow ischemia (perfused at 10% of baseline flow rate). The cardiac function was recorded with PowerLab Data Acquisition Systems. Lipid peroxidation was determined with Colorimetric/Fluorometric Assay Kit. The flux of glucose through the PPP and glycolysis was assessed by the contribution of the doublet (D23, [2,3-$^{13}C_2$]-lactate) and singlet (S3, [3-^{13}C]-lactate) to the total ^{13}C-NMR signal of lactate C3 in effluent, respectively.

Results

90min low-flow ischemia resulted in both systolic dysfunction (as indicated by decreased left ventricular systolic pressure, rate of tension development and developed pressure) and diastolic dysfunction (as indicated by increased end diastolic pressure and decreased rate of relaxation) accompanied with increased lipid peroxidation. Furthermore, the flux of glucose through PPP increased substantially and correlatively with that through glycolysis.

Conclusion

[1,2-$^{13}C_2$]-glucose can be used to simultaneously assess flux of glucose through PPP and glycolysis. The flux of glucose through both PPP and glycolysis increased during myocardial low-flow ischemia.

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