The Role of Autophagy During Myocardial Ischemia and Reperfusion Injury in Isolated Rat Hearts

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Introduction

Background

Coronary Heart Disease (CHD) is the leading cause of death and disability worldwide. Surviving an episode of myocardial infarction is associated with a high rate of subsequent cardiac events. Autophagy is a key cellular process for maintaining integrity and survival in various diseases. It involves the degradation of cytoplasmic contents by lysosomes under nutrient-deprived conditions. Previous studies have indicated that autophagy is involved in the prevention and treatment of myocardial infarction.

Objective

To examine if autophagy is beneficial or detrimental to myocardial infarction injury by measuring post-reperfusion cardiac function and infarct size when giving autophagy enhancers or inhibitors as either a pre-treatment or post-treatment compared to control I/R.

Hypothesis

Autophagy enhancement would be beneficial to cardiac function and decrease infarct size when given as a post-treatment similar to pre-treatment when compared to control I/R. By contrast, autophagy inhibition would exhibit compromised cardiac function and similar infarct percentage as control I/R.

Methods

Experimental procedures were according to the guidelines of the National Institutes of Health and the American Heart Association. Isolated rat hearts were subjected to 30 min of global ischemia followed by 20 min of reperfusion. The hearts were then subjected to 5 min of reperfusion. The effects of autophagy enhancers (e.g., rapamycin and trehalose) and inhibitors (e.g., 3-Methyladenine) were evaluated.

Results

Key Findings

- Autophagy enhancement improved cardiac function and decreased infarct size when given as a form of post-treatment, similar to pre-treatment.

- Autophagy inhibition showed a decrease in final LVDP compared to control I/R.

- Trehalose post-treatment did not show a significant decrease in infarct size compared to control I/R.

- Rapamycin pre-treatment showed an increase in final LVDP when compared to control I/R.

Conclusions & Implications

- Hearts treated with autophagy enhancers as pre-treatment or post-treatment both showed a decrease in infarct size percentage and an increase in cardiac function when compared to control I/R group.

- Hearts treated with an autophagy inhibitor as pre-treatment or post-treatment did not show a significant decrease in infarct size, and cardiac function was compromised similar as control I/R group.

Future Research

Future investigations will include:

- Evaluation of the synergistic effects of autophagy enhancers on cardiac function and infarct size when given as both pre and post-treatment.

- Evaluation of the change of autophagy induction markers by measuring LC3-2 and Beclin-1 (see figure 9) in an isolated hypoxia/re-oxygenation cardiomyocyte model.

- Evaluation of the effects of autophagy enhancers or inhibitors in isolated hypoxia/re-oxygenation cardiomyocytes model.

References


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