Introduction

Following an acute myocardial infarction, reperfusion of blood flow to the ischemic myocardium, although necessary, leads to compromised heart function resulting in MI/R injury. PKC epsilon positively regulates eNOS and reduces mitochondrial damage to reduce superoxide production. During I/R insult, PKC epsilon activates PKC (e.g., PKC epsilon) and inhibits uncoupled NO synthesis, which produces O$_2$- instead of NO resulting in vascular endothelial dysfunction. Activated PKC epsilon enhances eNOS activity and opens mitochondrial ATP-dependent potassium channels causing exacerbation of MI/R injury during reperfusion. By contrast, PKC epsilon translocation interacts with both substrates by binding to the PKC epsilon receptor for activated C kinase (RACK) domain [see Figure 1] to provide cardioprotective effects.

Hypothesis

We hypothesize that PKC epsilon-treated I/R hearts compared to untreated I/R hearts will exhibit improved post-reperfusion cardiac function and regional coronary flow.

Methods

Isolated Rat Heart Perfusion Preparation: Hearts were isolated from male Sprague Dawley rats (275-325g, Charles River, Springfield MA) via Langendorff heart preparation as previously described [4]. Experimental protocol was determined in the rat ventricle and this improvement in flow probably underlies the improvement in cardiac performance.

Determination of regional coronary flow using microspheres allows for a direct correlation between left ventricular coronary flow and left ventricular cardiac function. As evidenced by the data in Figure 3 coronary flow between PKC epsilon-treated I/R hearts and untreated I/R hearts were equivalent, yet regional flow in the left ventricle injected with microspheres was significantly increased in PKC epsilon-treated I/R hearts, see Figure 4. Our findings suggest that the ex vivo rat heart is sensitive to reductions in oxygen concentration in Krebs’ buffer. Such a decrease in levels of microspheres increase measure depression of cardiac function. Future experiments will determine the fluorescence in the single injection 45 min reperfusion.

Results

Untreated shams (i.e., no I/R) hearts without microsphere maintained cardiac contractile function throughout the experimental time period. By contrast, shams hearts that received triple microsphere injections showed a significant decrease in left ventricular developed pressure (LVPD) (i.e., left ventricular end-systolic pressure (LVEPS)) and this effect is attributed to a significant decrease in LVEPS and dP/dt max (Fig. 3).

Statistical Analysis: A student’s t-test was used to assess statistical differences in cardiac functions and microsphere fluorescence between I/R and I/R + PKC epsilon-treated I/R hearts. Probability values of p < 0.05 were considered statistically significant.

References


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