Conference Presentation

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Reducing the Incidence of Post - Myocardial Infarction Heart Failure in an Era of Improved Primary Percutaneous Coronary Intervention through Novel Therapeutics (Protein Kinase C Beta II Inhibitor)

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Abstract

Heart failure (HF) complicating myocardial infarction (MI) remains a major source of morbidity, mortality and a huge health-care burden in the world. The incidence of symptomatic HF after primary percutaneous coronary intervention (PPCI) has been widely reported. PPCI has improved early survival of MI, but its impact on downstream HF is deliberated. Infarct size is the major determinant of the development of HF and prognosis. Efforts to reduce the size will therefore have a significant impact on the incidence of HF after PPCI.

Resuscitation of the ischemic myocardium, heavily rests on timely reperfusion. However, cardiomyocyte death still occurs due to ischemic/reperfusion (I/R) injury mediated by oxidative stress. This phenomenon is known to largely contribute to the size of infarct. Activation by protein kinase C-βII (PKCβII) is attributed to the generation of reactive oxygen species (ROS) during this process and inhibition of this drive could salvage the myocardial tissue and subsequently preserve cardiac function. We hypothesized that myristic acid (Myr) and trans-activator of transcription (Tat) conjugated PKCβII inhibitor (Myr-Tat-PKCβII-) will exhibit robust cardioprotective effects in an in vivo porcine model, reflective of our ex vivo rat hearts model.

Male Yorkshire pigs underwent regional I/R by occluding the second branch of the left anterior descending artery (LAD). This was achieved in the catheterization laboratory guided by fluoroscopy. A bolus of Myr-Tat-PKCβII- or scrambled control was infused into the LAD during reperfusion. Cardiac function was evaluated by an echocardiogram during the entire procedure, and assessed as the relative change at the end of 3hr reperfusion compared to baseline.

Post-reperfused hearts were stained with Evans Blue dye to identify the area a risk and 1% triphenyltetrazolium chloride to delineate the area of necrosis. Infarct size and ejection fraction (EF) were analyzed via Student's t- test.

From mean baseline EF (61.4±0.5%), Myr-Tat-PKCβII- preserved EF with a relative change of 1.2±2.8% compared to 8.9±2.2% in control hearts ($p<0.05$) at the end of reperfusion.

Myr-Tat-PKCβII- reduced infarct size to 13.5±3.9% (n=4) compared to scrambled control hearts (27.5 ±7.9%, n=6). These results suggest Myr-Tat-PKCβII- significantly preserve EF after PPCI and reduce infarct size when given at reperfusion onset. This study gives a solid premise for future examination of Myr-Tat-PKCβII- in an 8 week in-vivo, porcine MI survival study.

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