Periodic Acceleration (pGz) after Cardiac Arrest Restores Antioxidant Capacity in Swine Hearts

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Introduction

- Cardiac Arrest (CA) and Resuscitation are models of whole body ischemia reperfusion injury (I/R)
- Oxidative Stress and Decreased Antioxidant Capacity are hallmarks of all models of I/R and CA
- Increased Oxidative stress after I/R has been shown
  - in cellular, and animal models,
  - as well as human subjects.
Whole Body Periodic Acceleration (pGz) is the sinusoidal head to foot motion of the supine body, which has been shown to induce pulsatile shear stress to the vascular endothelium. (J Appl Physiol (1985). 2009;106:1840-7, Critical care medicine. 2001;29:1983-8., Annals of biomedical engineering. 2003;31:1337-1346.)
• **We have previously shown that:**
  
  
  

• **In vivo and in vitro pGz has also been shown to:**
  
  
Hypothesis

We hypothesized that pGz performed after CA and resuscitation in a well established pig model of CA, may restore antioxidant capacity in heart.
Experimental Protocol Schematic

Conventional Ventilation (CONT) (n=17)*

CONTROL(CONT)(n=7)

pGz (CPR-pGz) (f=3 Hz G ± 0.4 m/sec)(n=7)

ROSC 2 hrs

ROSC 30 mins

8 min VF CPR Defibrillation

BL

CA

Myocardium Harvest
Catalase
SOD–Superoxide Dismutase
GPX–Glutathione Peroxidase
GSS–Glutathione
GSSH

* 3 animals served as SHAM
Methods

• Hemodynamics and Blood Gases
• Echo at Baseline (BL) 30 and 120min after pGz
• Myocardial Tissue
  – SOD, CAT, GPx, GSS, GSSH
• Cellular Data- Cardiomyocyte
  – Hypoxia Re-oxygenation cardiomyocyte model
Summary of Animal Results

• All Animals Survived
• Median Number of Defibrillation attempts =4
• Blood gases before, during and after resuscitation were not different between groups
• Hemodynamics: Blood pressure, and CPP were not different between groups
  – Pulmonary Artery Pressure was significantly lower in pGz treated animals
Antioxidants
Hypoxia was induced by superfusing the cardiomyocytes with a solution without glucose and saturated with 95%N₂–5% CO₂ for 30 min.

Re-oxygenation was induced by perfusing the cardiomyocytes with a solution aerated with 95%O₂ – 5% CO₂ for 30 min.

**Cellular Experimental Protocol Schematic**

**BL**

- Hypoxia

- Determination of [Ca²⁺]_d and ROS production

**REOXYGENATION (CONT)(n=7)**

(pGz)

- Determination of [Ca²⁺]_d and ROS production

**Detonation of [Ca²⁺]_d and ROS production**

ROS=dichlorodihydrofluorescein diacetate (DCFH-DA)

Ca= double/barreled Ca²⁺-selective microelectrodes
Brain Homogenates

![Graph showing protein expression levels for different groups (Sham, CONT, CPR-pGz) for CAT, SOD, GPx, and Tubulin. The graph indicates statistically significant differences marked with asterisks.](image-url)
Conclusions

- Our data confirms our previous findings of decreased myocardial stunning with pGz after CA
- CA decreases Antioxidant Defense and pGz restores it
  - The effect of pGz on antioxidants appears to be systemic in nature
- Cellular data confirms that I/R
  - Increases ROS production
  - Decreases Antioxidant Defense
  - pGz restores Antioxidant Defense and decreases ROS production
- Nuclear Translocation of NRF₂ appears to signal pGz induced increase in antioxidant defense.
- In conjunction with our previous findings pGz is a novel method to harness endogenous Antioxidant Defense and a new post-resuscitation care strategy to reduce effects of oxidant damage and decrease inflammatory response
Thank you

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