

NF- κ B Inhibition Improves Recovery from Ischemia/Reperfusion in a Neonatal Piglet Model.

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BACKGROUND: Congenital heart disease is the most prevalent birth defect and the leading cause of death within the first year of life. Unfortunately, operative repair often requires the use of cardiopulmonary bypass (CPB) and deep hypothermic cardiac arrest (DHCA). This procedure often generates ischemia and reperfusion injury mediated by nuclear factor kappa B (NF- κ B). Our hypothesis is that NF- κ B inhibition can alleviate the cardiopulmonary dysfunction associated with ischemia and reperfusion injury following CPB.

OBJECTIVES: SN50 is a peptide which prevents NF- κ B nuclear translocation. Here we want to determine the degree to which SN50 can reduce cardiopulmonary bypass induced inflammation and improve cardiopulmonary function.

METHODS: Two week old piglets received 100 μ g/kg of SN-50 1 hr before CPB. The animals are cooled to 18°C with CPB after which the CPB is turned off. The piglets remain in DHCA for 120min and then are rewarmed to 38°C. Three sets of sonomicrometric crystals and 3 pressure catheters were used to collect hemodynamic data over the next 120 min. Transmural left and right ventricular tissues were obtained at the terminal time point. NF- κ B (p50+p65) activity was determined using ELISA. The control group received saline. Data expressed as mean \pm SD.

RESULTS: There was a 56% reduction in NF- κ B activity in the SN-50 treated animals compared to the untreated group (p=0.004). Oxygen delivery was maintained at 73 \pm 17 ml/min at baseline and 78 \pm 6 ml/min at 120 min (p=0.75) in the treated animals vs. 99 \pm 26 ml/min at baseline and 63 \pm 20 ml/min at 120 min (p=0.0001) in the control group. Pulmonary vascular resistance (dynes \cdot s/cm⁵) increased from 124 \pm 59 at baseline to 369 \pm 232 at 120 min (p=0.001) compared to SN-50 treated animals 105 \pm 34 to 99 \pm 24 at 120 minutes (p=0.09).

CONCLUSION: There is evidence that the improvement of cardiopulmonary function after ischemia/reperfusion is mediated through the inhibition of NF- κ B activity in piglets. Treatment with SN50 improved systemic oxygen delivery, and significantly reduced pulmonary hypertension in piglets undergoing CPB-DHCA. Selective inhibition of NF- κ B may be a potential therapy for reducing ischemia/reperfusion injury after pediatric cardiac surgery.