

Optimizing Nicorandil for Spinal Cord Protection in a Murine Model of Complex Aortic Intervention

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INTRODUCTION

- There are currently no pharmacological agents utilized to increase metabolic tolerance to spinal cord ischemia-reperfusion injury in the setting of complex aortic surgery.
- Nicorandil, a ATP-sensitive potassium (KATP) channel opener, has shown promise in neuroprotection.
- *We hypothesized that 3 days of Nicorandil pretreatment confers effective neuroprotection via activation of the mitochondrial KATP channel.*

MATERIALS AND METHODS

- Spinal cord injury was induced by 7 minutes of thoracic aortic cross clamping in adult male C57BL/6 mice.
- Limb motor function was evaluated, viable anterior horn neurons quantified.

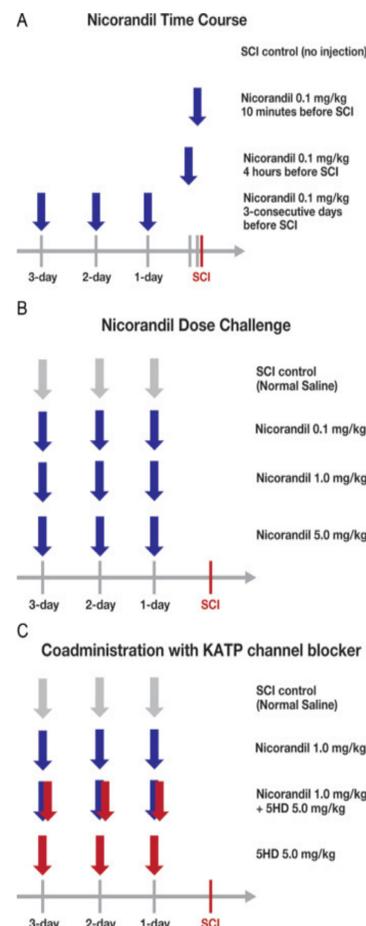


Figure 1: Experimental design for each group. (A) Nicorandil time course. (B) Nicorandil dose challenge. (C) Coadministration with KATP channel blocker.

RESULTS

- Nicorandil pretreatment at 4 hours and 3 days before ischemia significantly preserved motor function preservation.
- All Nicorandil doses showed significant motor function preservation.
- Neuroprotection was abolished by 5HD co-administration.
- Histological analysis showed significant neuron preservation with Nicorandil pretreatment, quantified with NeuN staining.

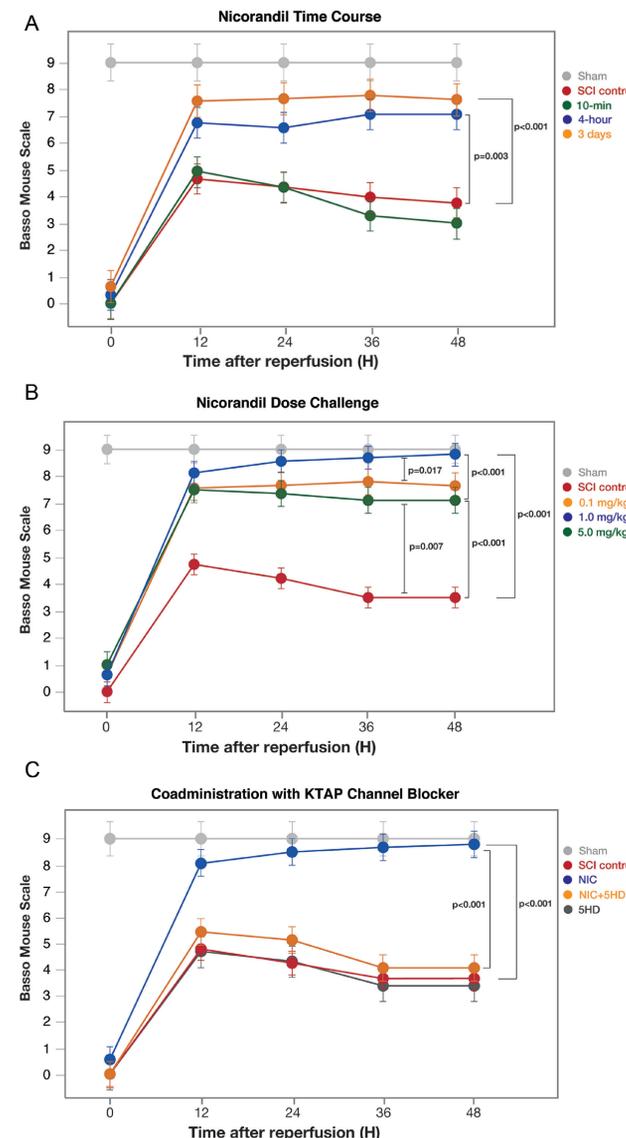


Figure 2: Mouse limb motor function after ischemia-reperfusion injury for each group is expressed as least square mean ± standard error.

CONCLUSIONS

- Three days administration of Nicorandil 1.0 mg/kg showed near-total motor function preservation in a murine spinal cord ischemia-reperfusion model, mediated by the mitochondrial KATP channel.
- Further elucidation of the Nicorandil effect through KATP pathway is needed, unclear if acts through direct or indirect pathways.
- Nicorandil is a promising clinical and pharmacologic agent that may improve patient outcomes in the setting of complex aortic surgery.

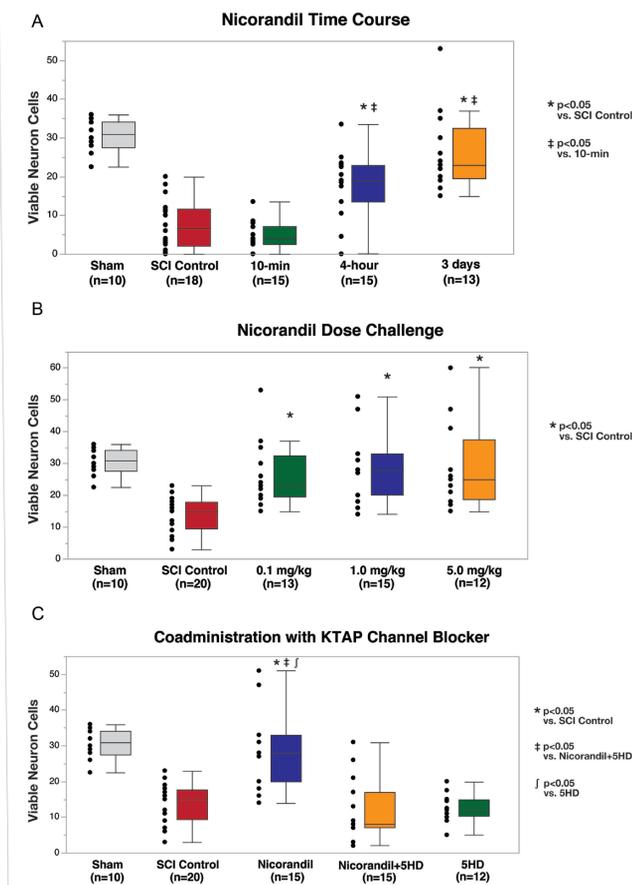


Figure 3: Number of viable neurons within a standardized section of the anterior horn of the spinal cord for each group using NeuN staining (10x magnification).

Acknowledgements & Disclosures

Conflicts of Interest: None declared

Funding Statement: Funding for this project was allocated through the division of Cardiothoracic Surgery at the University of Colorado Anschutz Medical Campus.

Acknowledgements: Hirokazu Hashimoto, MD., PhD., Department of Cell and Developmental Biology, University of Colorado, contributed to the procedural development of the NeuN staining for viable neuron cells and western blotting for the pAKT activation.

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