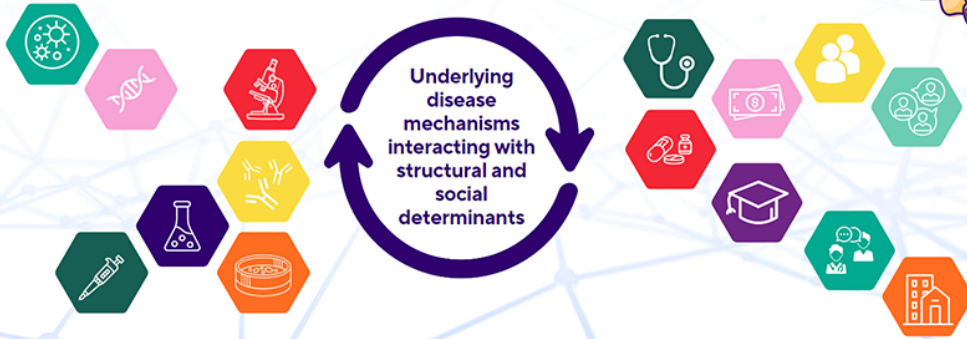




19TH ANNUAL CHILD HEALTH RESEARCH DAYS
Outcomes in Child Health



October 25 + 26, 2023 | RBC Convention Centre, Winnipeg, Manitoba

Abstract Submission Form

CHR D 2023: Abstract Submission Form

Submitter Name

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Presenter Name

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Presenter Status

Undergraduate Students

Research Category

Basic Science

Role in the project

Design
Perform Experiments
Analyze Data
Write Abstract

Title

NO and 100% O₂ treatment sensitize the contractile pathway in hypoxia-induced PPHN

Background

Persistent Pulmonary Hypertension of the Newborn (PPHN), a failure of pulmonary circulatory transition, triggers ~10% of NICU admissions and has a 10-20% mortality rate. Hypoxia-induced pulmonary vasoconstriction is managed with Nitric Oxide (NO) and 100%O₂. However, 25-30% of cases don't respond or develop NO resistance. Treatment with NO and 100% O₂ may lead to an increase in reactive oxygen species (ROS) and nitrogen species (RNS). We hypothesized that this combination can worsen pulmonary vasoconstriction.

Objective

To investigate the effect of NO and 100% O₂ on the thromboxane receptor (TP) mediated vasoconstrictor pathway.

Methods

Porcine resistance-level pulmonary arterial smooth muscle cells were cultured and subjected to normoxia or hypoxia for 72 hours with or without treatment of 1uM Sodium Nitroprusside (SNP; an NO donor) and 2hrs of 100%O₂. Addition of FeTPPS, a peroxynitrite scavenger, was also studied. Calcium mobilization was measured using FURA-2AM; Western blot and immunoprecipitation was used to determine abundance and association between thromboxane receptor (TP) and Gαq, respectively.

Results

Treatment didn't alter cell survival. TP-mediated Ca²⁺ mobilization increased 2x following hypoxia; addition of 100% O₂ and SNP further elevated Ca²⁺ response to 3x that of controls. This hyper-reactivity was ablated with the addition of FeTTPS. Abundance of TP and Gαq were unchanged. However, hypoxia moderately, but significantly elevated TP-GαQ coupling. In both control and hypoxic cells, treatment with 100% O₂ and SNP increased coupling by 1.5x; FeTTPS attenuated this.

Conclusion

The contractile pathway appears to be sensitized by treatment with 100% O₂ and SNP after hypoxic preconditioning. While 2 hours of 100% O₂ with NO is a routine clinical practice, our evidence suggests that this treatment may biochemically sensitize pulmonary vasoconstrictive pathways. This elucidates a mechanism for PPHN treatment failure, suggesting further investigations into appropriate PPHN management.

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