2023 Annual Research Day Poster Sessions – April 19th, 2023

Session/Poster#	Presenter
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Influence of Neonatal Intermittent Hypoxia Paradigms on Inflammatory Biomarkers of Necrotizing Enterocolitis in the Rat Terminal Ileum.

Despite major advances in neonatal care, necrotizing enterocolitis (NEC) continues to be the leading cause of gastrointestinal (GI)-related death in extremely low gestational age neonates (ELGANs). During oxygen therapy, ELGANs frequently experience intermittent hypoxia (IH) episodes followed by hyperoxia episodes between events resulting in oxidative stress and inflammation which are hallmarks of NEC. Toll-like receptor (TLR)-4 and intestinal fatty acid binding protein (iFABP) have been identified as early diagnostic biomarkers of NEC.

We tested the hypothesis that neonatal IH resolving with normoxia is less injurious to the immature terminal ileum than IH resolving in hyperoxia between episodes. Injury was confirmed by a composite of histopathology, apoptosis, levels of inflammatory markers, and TLR-4 in the terminal ileum.

Newborn rats at birth (P0) were exposed to: Hyperoxia (Hx, 50% O2) with brief hypoxia (12% O2); Room air (RA) with hypoxia; Hyperoxia with RA (intermittent hyperoxia or IHx); Hyperoxia only; or RA only, from P0 to P14. Pups were studied at P14 for immediate effects, or placed in RA until P21 for recovery/reoxygenation. Terminal ileum samples were assessed at P14 and P21 for histopathology, apoptosis, cytokines (IL-1Î², IL-6, TNFÎ±, TGFÎ²), TLR-4, iFABP, and epidermal growth factor (EGF).

Hx, IHx, and both IH paradigms resulted in significant damage to the terminal ileum with many characteristics consistent with NEC. The histopathological changes persisted after recovery in RA. Similar outcomes were noted for apoptosis and elevations in the expression of NFkB. TLR-4, iFABP, and all cytokines increased with the Hx, IHx, and both IH paradigms, while EGF significantly declined.

The immature terminal ileum is highly susceptible to changes in oxygen regardless of normoxia or hyperoxia recovery. TLR-4 and iFABP remain valid biomarkers of intestinal damage. Interventions to curtail O2 variations should remain a high priority to prevent NEC.