Background

- Bronchopulmonary dysplasia (BPD) is a common morbidity of prematurity associated with neonatal mortality, pulmonary hypertension and persistent pulmonary dysfunction into adulthood.
- Preeclampsia (PE) and chorioamnionitis (CA) are known risk factors the development of BPD but the specific mechanisms have not yet been clearly defined.
- Serum levels of maternal soluble fms-like tyrosine kinase (sFlt-1), a VEGF antagonist, are associated with PE severity and inversely correlated with GA and birth weight.
- Maternal Vitamin D (Vit D) deficiency is also associated with multiple adverse pregnancy outcomes including preeclampsia, gestational diabetes, and low birth weight2
- We have previously shown that antenatal Vit D treatment decreases pup morbidity, improves placental vasculature and improves lung development in a rat model of CA.
- We have also previously shown that IA sFlt exposure decreases pup weight and alters distal lung development and function.
- It is not yet known if antenatal Vit D therapy has a protective role in the sFlt induced model of PE associated BPD.

Study Questions

1. Will IA Vit D treatment restore lung architecture and vascular development?
2. Will IA Vit D treatment restore lung function in sFlt exposed animals?

Hypothesis

IA Vit D treatment will attenuate lung injury after IA sFlt exposure.

Methods

Study Design

- q2D Term (e22)
- Control (Saline)
- sFlt (1.5 µg)
- sFlt (1.5 µg) + Vit D (50 pg)
- Vit D (50 pg)

Antenatal Injections

- C-section Delivery
- Maintained in Room Air
- Day 14

Analysis Performed at Day 14

- Lung Morphometrics
- Right Ventricle Hypertrophy
- Right Ventricle Hypertrophy
- Pulmonary Function

Lung Morphometrics

- Whole lungs harvested and inflated to 20 cmH2O
- H&E stain: Radial Alveolar Counts
- CD31+ immunohistochemistry: Pulmonary Vessel Density

Right Ventricle Hypertrophy

- Left Ventricle plus septum (LV+S) and Right Ventricle (RV) were dissected and weighed

Pulmonary Function

- Pups were anesthetized and cannulated via tracheotomy
- Single compartment lung compliance and resistance assessed via Flexivent system

Results

Antenatal Vit D Treatment Improves Vessel Density and Prevents Right Ventricular Hypertrophy in sFlt Exposed Animals

Antenatal Vit D Treatment Improves Alveolarization in sFlt Exposed Animals

Summary

1. Antenatal sFlt exposure decreases lung structure and function.
2. Antenatal Vit D treatment improves distal lung architecture.
3. Antenatal Vit D treatment restores pulmonary vessel density and prevent rights ventricular hypertrophy.
4. Antenatal Vit D treatment improves lung function in the neonatal rat lung.

Conclusions

- Antenatal Vitamin D treatment improves distal lung morphology and vascular development.
- Antenatal Vitamin D treatment restores neonatal rat pulmonary function.

Speculations

- Vitamin D treatment restores lung development through improved pro-angiogenic signaling in the fetal lung.
- Optimization of fetal and neonatal Vitamin D levels can improve pulmonary development and function.

References

2) Dhir D, Curr Opin Obst Gyn 2011
4) Kovacs CG et al. Am J Endo Metab 2005
6) Olmos-Drito et al. Nutrients 2015