Chloride Channel Protein Abundance is Persistently Elevated during Evolution of Neonatal Chronic Lung Disease in Preterm Lambs

L Deneckere, N Brewster, MJ Dahl, L Dong, ZM Wang, BA Yoder, DM Null, DP Carlton, and KH Albertine
Disclosure Statement

Laura Deneckere does not have anything to disclose
Fetal Lung Architecture

- Normal fetal development
  - Canalicular or saccular stages

Human Distal Lung Architecture

22 weeks gestation  32 weeks gestation

http://o.quizlet.com
Ion Transport: Fetal Lung *In Utero*

- Net chloride (Cl⁻) secretion predominates
- Apical chloride (Cl⁻) intracellular channels (CLIC)
- Net liquid flow from blood to potential airspaces

Ion Transport: Labor and Postnatally

- Ion transport switches from net Cl\(^-\)-secreting to net sodium (Na\(^+\))-absorbing epithelium
  - Basolateral Na\(^+\), K\(^+\)-ATPase pump activity
  - Reverses direction of net liquid flow

Preterm Birth and Neonatal Lung Injury

- Preterm birth is frequently associated with
  - Respiratory distress that requires intermittent mandatory ventilation
    - Neonatal acute lung injury
      - Interstitial and airspace edema
        - Airspace edema is the result of net liquid imbalance across the epithelial barrier
Unknown

If protein abundance of Cl⁻ channels and Na⁺, K⁺-ATPase pumps is affected differently by ventilation mode used to support preterm neonates

Hypothesis

Protein abundance of Cl⁻ channels and Na⁺, K⁺-ATPase pumps is affected differently by ventilation mode used to support preterm lambs
Preterm Lamb Model

- Antenatal steroids

Delivered at ~131 days
(Term is ~150 days)

Intubated and treated with surfactant and caffeine citrate

Intermittent mandatory ventilation (IMV) ~3 hours

- Invasive IMV
  (Dräger Babylog VN500 ventilator
  5-7 mL/Kg tidal volume)

- Less-invasive HFNV
  (Percussionaire® ventilator)

3 or 21 days

HFNV, high-frequency nasal ventilation
Management

❖ Preterm lambs

● During ventilation
  ● PaO₂ 60-80 mmHg
  ● PaCO₂ 45-60 mmHg
  ● pH 7.25-7.45
  ● Treated with antibiotics
  ● Enteral feedings, using ewe’s colostrum and milk, starting at 3 to 4 h of life
  ● Plasma glucose 60-90 mg/dL
Analyses

- Immunoblot
  - Cl⁻ channels
  - Na⁺, K⁺-ATPase pumps
More Cl⁻ Channel Protein at 3d of IMV

Relative Protein Abundance (Normalized MemCode)

Mean ± SD; n=4

* p<0.05 compared to PT3d HFNV
† p<0.05 compared to F134
More $\text{Na}^+$, $\text{K}^+$-ATPase Pump Protein at 21d of IMV

Mean ± SD; n=4

* $p<0.05$ compared to PT21d HFNV

† $p<0.05$ compared to T1d
Na\textsuperscript{+},K\textsuperscript{+}-ATPase $\beta$ Immunolocalization, 3d

F131

Preterm 3d

Invasive

IMV

Less-invasive

HFNV
Na⁺,K⁺-ATPase β Immunolocalization, 21d

F131

T1d

Preterm 21d

Invasive IMV

Less-invasive HFNV
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* Compared to less-invasive HFNV and unventilated reference lambs
### Summary for Protein Abundance

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Conclusion

- Protein abundance of Cl⁻ channels and Na⁺, K⁺-ATPase pumps is disrupted during invasive IMV
Speculation

- More protein abundance of Cl⁻ channels at 3d of invasive IMV
  - May contribute to wetter lungs
    - Necessitate higher inspired oxygen and airway pressures

- More protein abundance of Na⁺, K⁺-ATPase pump at 21d of invasive IMV
  - May be a compensatory response to dry the lung’s parenchyma
Thank you

Supported by
HL110002
HL062875
LU-R1 Program (Lawrence University)