Mechanism of reduced lung injury by high-frequency nasal ventilation in a preterm lamb model of neonatal chronic lung disease.

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ABSTRACT:

The mechanism underlying the potentially beneficial effects of the "gentler" modes of ventilation on chronic lung disease (CLD) of the premature infant is not known. We have previously demonstrated that alveolar parathyroid hormone-related protein-peroxisome proliferator-activated receptorγ (PTHrP-PPARγ) signaling is critically important in alveolar formation, and this signaling pathway is disrupted in hyperoxia- and/or volutrauma-induced neonatal rat lung injury. Whether the same paradigm is also applicable to CLD, resulting from prolonged intermittent mandatory ventilation (IMV), and whether differential effects of the mode of ventilation on the PTHrP-PPARγ signaling pathway explain the potential benefits of the "gentler" modes of ventilation are not known. Using a well-established preterm lamb model of neonatal CLD, we tested the hypothesis that ventilatory support using high-frequency nasal ventilation (HFNV) promotes alveolar PTHrP-PPARγ signaling, whereas IMV inhibits it. Preterm lambs managed by HFNV or IMV for 21 d following preterm delivery at 132-d gestation were studied by Western hybridization and immunofluorescence labeling for key markers of alveolar homeostasis and injury/repair. In lambs managed by IMV, the abundance of key homeostatic alveolar epithelial-mesenchymal markers was reduced, whereas it was significantly increased in the HFNV group, providing a potential molecular mechanism by which "gentler" modes of ventilation reduce neonatal CLD.

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