Mechanical Ventilation of Newborn Mice: Effects on Lung Development Genes

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Rationale: Failed formation of alveoli and lung capillaries is a key histological feature of neonatal chronic lung disease (CLD). CLD typically afflicts premature lungs exposed to lengthy mechanical ventilation (MV) with O2-enriched gas.

Objective: As lung septation and angiogenesis occur mainly after term birth in mice, we did studies to see if MV with 40% O2 would alter lung expression of genes that regulate alveolar and lung vascular development in newborn mice. Methods: We studied 3 groups of 8 pups that were 2-4d old and weighed 2-4g. Group 1 had a tracheotomy followed by MV with 40% O2 for 8h at 60 breaths/min (bpm), peak inflation pressure (PIP) 17±1, mean airway pressure (MAP) 4±1 cmH2O. Group 2 had a tracheotomy followed by MV with 40% O2 for 8h at 180 bpm, PIP 11±2, MAP 4±1 cmH2O. Group 3 (Control-no MV) had sham surgery, then breathed 40% O2 for 8h. Lungs were frozen for later microarray analysis and quantitative RT-PCR to measure mRNA for genes considered important in lung development (Vascular Endothelial Growth Factor A, VEGF-A, and its receptor, VEGF-R2; Tenascin-C, TN-C; and Lysyl Oxidase, LO). Some lungs were processed for histology, which showed no evidence of injury in the 3 groups. Results: Microarrays and qRT-PCR showed 30-35% less (p<.05) lung expression of VEGF and VEGF-R2 and >2-fold more LO in Groups 1 and 2 than in Group 3 (control). TN-C was >50% less (p<.05) in Group 2 than 3, but not significantly different in Groups 1 and 3. Conclusion: A prolonged period of cyclic lung inflation with O2-enriched gas at a critical stage of development, even without apparent lung injury, may impact lung expression of genes that regulate alveolar and lung vascular formation.

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