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| **Developing an extremely preterm lamb model for preterm lung-brain axis studies.** |
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| **Introduction/Aim:** Preterm lambs born at 125-128d (85% of full-term) have saccular lungs and develop respiratory distress. However, the 128d fetal lamb brain approximates near-term human brain development. Therefore, we aimed to determine if preterm lambs with canalicular lung development may be viable as a postnatal preterm lamb model to assess the more preterm lung-brain axis.**Methods:** Time-mated merino ewes (n=22) received antenatal intramuscular (IM) medroxyprogesterone (150 mg/kg) at 104d gestation, followed by two doses of IM betamethasone (11.4mg) administered 10d and 5d prior to lamb delivery at 124d (n=10), 121d (n=11), 118d (n=11) and 115d (n=10) gestation. Lambs were surgically delivered, received intra-tracheal surfactant (100mg/kg), and were mechanically ventilated for 3h to evaluate their physiological stability and lung function. Lung injury and inflammation were assessed using H&E stain and immunohistochemistry. Group differences were compared using 1 or 2-way ANOVA with Tukey’s post-hoc test.**Results:** All lambs survived 3h of ventilation, except for one lamb in the 115d group. Gas exchange progressively worsened with decreasing gestation; the 115d group required the highest levels of supplemental oxygen (FiO2, p<0.001 vs. all groups) and displayed the poorest alveolar-arterial gas transfer (p<0.0001 vs. all groups). Indices of lung function were similarly reduced in 115d lambs, including dynamic compliance (Cdyn, p<0.0001) and ventilation efficiency index (p<0.0001). Lung injury scores were not different between groups (p=0.09). Surprisingly, lung inflammation (CD45) was highest in the 121d group (p<0.05 vs. all groups).**Conclusion:** Preterm lambs can be delivered as early as 115d gestation and managed postnatally for 3h with ventilation support. The feasibility of using 115d (75 %) gestation lambs in longer postnatal studies requires evaluation. However, our ovine canalicular lung model provides a closer representation of extremely preterm infants and may improve clinical relevance for studies of the preterm lung-brain axis.**Grant Support:** GNT1196188 |