

DOSE-RESPONSE TO AEROSOLIZED KL₄ SURFACTANT IN THE SPONTANEOUSLY BREATHING CPAP-SUPPORTED PRETERM LAMB

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Background: We have demonstrated effectiveness of an aerosolized, peptide-containing, synthetic surfactant (KL₄ surfactant), in spontaneously breathing CPAP-supported preterm lambs. Dose-ranging studies are required to define the dose that produces optimal physiologic and biomarker responses.

Aims: To evaluate dose-responses to aerosolized KL₄ surfactant using lung mechanics, histomorphology and lung inflammation biomarkers in spontaneously breathing, CPAP-supported preterm lambs.

Methods: Following Cesarean section, lambs (n = 20; 130-132 days gestation) were anesthetized, instrumented, delivered, supported with 100% oxygen, CPAP, and caffeine then quasi-randomized to receive CPAP alone (controls) or CPAP plus aerosolized KL₄ surfactant for up to 10, 20, 30 or 90 min. exposure at 1.2 mL/min. Cardiopulmonary parameters were monitored for 4 hrs. Lung IL-8 and histomorphometry were also measured.

Results: Compliance increased and lung IL-8 decreased in an aerosolized KL₄ surfactant dose-dependent manner relative to CPAP treatment alone. Marked differences occurred with the 20 min dose vs. CPAP alone with little differences between the 20, 30 and 90 min. doses. PaO₂ was greater than in controls following the 10, 20 and 30 min. doses and trended towards control values with the 90 min. dose. Gross and histomorphometry lung assessment demonstrated greater and more homogenous expansion compared to controls, independent of treatment duration.

Conclusions: Aerosolized KL₄ surfactant improved gas exchange, pulmonary mechanics, lung structure integrity, and reduced lung inflammation in a dose-dependent manner relative to treatment with CPAP alone. These observations provide preliminary guidance for titrating dosing strategies for optimal management of RDS.(Discovery Laboratories, Inc; DURIP-ONR; NIH P20 RR 020173).