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Evaluation of intra-amniotic surfactant administration for lung maturation in preterm sheep

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Abstract

We aimed to evaluate the effects of intra-amniotic surfactant administration on alveolar lecithin/sphingomyelin ratio, density of type II pneumocytes, and fetal lung function in preterm merino sheep. Pregnant ewes at 119 days gestation either received 200 mg intra-amniotic surfactant ($n = 4$) or saline solution ($n = 4$). After 24 h, the lambs were delivered by hysterotomy and mechanically ventilated. Lecithin/sphingomyelin ratios in alveolar fluid, inflating pressure–volume relationships, and type II pneumocyte counts in histological specimens were compared among the groups. All of the lambs completed the protocol. Mean lecithin/sphingomyelin ratio increased significantly in amniotic ($p = 0.03$) and alveolar fluid ($p = 0.03$) samples of surfactant-treated animals. Lung function in terms of pressure–volume curves did not differ between two groups. Type II pneumocyte density tended to be higher ($p = 0.057$) after intra-amniotic surfactant administration. Single-dose treatment with intra-amniotic surfactant seems to improve amniotic and alveolar lecithin/sphingomyelin ratio

Abbreviations: RDS, respiratory distress syndrome; L/S ratio, Lecithin to sphingomyelin ratio; SD, standard deviation

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questionably by increasing alveolar type II cells. Pressure–volume relationships from inflation of the lungs might be unaltered with intra-amniotic surfactant treatment.

Keywords: Intra-amniotic surfactant; Lung maturation; Preterm labor; Respiratory distress syndrome; Merino sheep

Introduction

Fetal lung development in mammalian species is divided into the pseudoglandular, canalicular, and terminal sac stages. During the pseudoglandular period, airways along with arteries and veins develop from a gland-like appearance to a pattern similar to that found in the adult. The emergence of the acinus, epithelial differentiation with the development of the potential air-blood barrier, and the beginning of surfactant synthesis within identifiable type II cells are three key incidents occurring throughout canalicular period. During the terminal sac (saccular) stage, final branching of the air spaces takes place. Finally, alveolarization is usually characteristic for late gestation and is initiated from the terminal saccules by the emergence of septa together with collagen and elastin fibers along with capillaries.

Surfactant contains 70–80% phospholipids, about 10% neutral lipids, and about 10% protein in all mammalian species. The principal phospholipid is saturated phosphotidylcholine (lecithin) acting as the primary surface-active component of surfactant. The composition of the phospholipids in the surfactant lipoprotein complex changes as gestation advances. Hence, saturated phosphotidylcholine can be utilized as a relatively precise determinant of surfactant metabolism. Surfactant is synthesized in and secreted by type II cells as a result of complex sequential biochemical events. Following the synthesis from choline, fatty acids, glucose, and phosphate mainly in the endoplasmic reticulum, surfactant is stored in type II cells as lamellar bodies. Contrary to synthesis, secretion typically occurs with the initiation of ventilation following birth (Jobe, 1994).

Exogenous surfactant administration to preterm neonates leads to improved ventilation and oxygenation of arterial blood (Zurawski et al., 2002). Infants treated with surfactant seem to have normalized central nervous and respiratory system development compared to non-treated controls (Zurawski et al., 2002). However, intraventricular brain hemorrhage risk might be increased especially after rapid bolus installation of surfactant probably due to altered cerebral blood flow pattern (Raju and Langenberg, 1993). Pulmonary parenchymal bleeding, pneumothorax, and bronchopulmonary dysplasia might also occur following surfactant therapy indicating possible lung damage (Raju and Langenberg, 1993; Zurawski et al., 2002). Whether such adverse effects are secondary to bolus exogenous administration of surfactant is a concern.

Prophylactic intra-amniotic administration of surfactant might provide a more physiological mode of delivery of surfactant into the fetal lungs. Fetal breathing