Expanded role of the surfactant system in perinatal transition

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The role of surfactant as an etiological factor of RDS is well known. Besides the surface activity, several components of the surfactant are involved in the innate immunity. The fact that surfactant is secreted into the amniotic fluid makes it as an interesting candidate that influences the premature birth, particularly in pregnancies complicated by chorioamnionitis. Surfactant associated collectins, surfactant protein A (SP-A) and SP-D are well known proteins that bind several microbes, influence phagocytosis by alveolar macrophages, and have pro- and anti-inflammatory roles. We have studied the roles of lung collectins using two approaches: 1. transgenic mice expressing either SP-A or SP-B are studied in the setting of LPS-induced preterm birth; 2. the association of SP-A and SP-D polymorphism with the susceptibility to preterm birth is studied. Preliminary results are presented. In addition new results on the role of SP-C in preterm birth are shown. According to preliminary evidence certain SP-C gene (SFTPC) polymorphisms associate with lung diseases and very preterm birth (Lahti et al. Eur J Hum Gen 2004;12:312-20).

Aims: We investigated the association of SFTPC single nucleotide polymorphism (SNP) rs4715 with factors affecting spontaneous preterm birth and characterized the SP-C expression in human and mouse gestational tissues.

Methods: SFTPC SNP rs4715 polymorphism was genotyped in a homogeneous Northern European population of mothers and infants in spontaneous preterm birth and term controls. The expression and protein of SP-C in gestational tissues was analyzed.

Results: SFTPC SNP rs4715 did not associate with spontaneous preterm birth. However, fetuses with short interval (< 72 hours) between preterm premature rupture of fetal membranes (PPROM) and preterm birth had significant overrepresentation of the minor allele A, whereas in fetuses with prolonged PPROM (≥ 72 hours) the frequency was decreased (P<0.0001). Maternal SFTPC did not associate with the duration of PPROM. SP-C mRNA and proprotein were detected in fetal membranes, placenta, and pregnant uterus.

Conclusion: SFTPC SNP rs4715 associates with the duration of PPROM and SP-C is expressed in gestational tissues. We propose that fetal SFTPC either moderates the inflammatory activation or serves as an antimicrobial peptide protecting the extraembryonic compartment.
Surfactant therapy for respiratory distress syndrome

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Respiratory distress syndrome (RDS) is a significant cause of morbidity and mortality in preterm infants. Surfactant therapy has made a significant impact on the survival without increasing the cost per survivor. Animal derived surfactants (ADS) as well as synthetic surfactants without proteins have been extensively evaluated in preterm infants. ADS are more effective and decrease mortality when compared to synthetic surfactants. Three ADS commonly available globally include Survanta (beractant), Infasurf (calfactant), and Curosurf (poractant alfa). They differ in their composition, amount of phospholipids and plasmalogens, onset and duration of action, dosing volume, viscosity, need for additional doses, clinical outcomes, and cost effectiveness. Prospective as well as retrospective studies comparing beractant and calfactant have shown no significant differences in clinical or economic outcomes. However, comparison of beractant with poractant alfa in randomized trials have shown significantly faster weaning of oxygen, fewer additional doses, decreased mortality and cost benefits in favor of poractant alfa. Differences in mortality reported from 10 studies have shown that poractant alfa is the only animal derived surfactant with a significant reduction in mortality when compared with beractant or calfactant. A retrospective study involving more than 24,000 preterm infants has shown a significant reduction in mortality, length of stay, and total hospital costs with poractant alfa when compared to beractant or calfactant. These differences in outcomes may be related to the fact that poractant alfa contains greater amounts of phospholipids distributed in a smaller volume as well as a greater amount of antioxidant phospholipids, namely plasmalogens.
Pulmonary function in newborns with meconium aspiration syndrome

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Meconium aspiration syndrome (MAS) is one of the most frequent causes of respiratory insufficiency and morbidity among term newborns. Reduction of the incidence and severity of MAS became a new target for obstetricians and neonatologists. Pathologic examinations of lungs from newborns who died of MAS a deficiency of surfactant was found as a result of secondary damage of pneumocytes type II function and the inhibition of biophysical properties of surfactant. Inflammation and surfactant inactivation may finally result in adult respiratory distress syndrome as well as predisposition toward persistent pulmonary hypertension of the newborn, a complication that may require ECMO. Thus it has been proposed that surfactant replacement in MAS may reverse respiratory insufficiency. Previous studies showed that conventional surfactant administration reduces the severity of MAS and, thus, decreases the number of infants with progressive persistent pulmonary hypertension of the newborn requiring support with ECMO. Also, other studies support the thesis that diluted surfactant lung lavage is a safe and potentially effective therapy in the treatment of infants with MAS.

Pulmonary function in MAS and changes in pulmonary mechanics during treatment were not clearly described, and no objective values of pulmonary functions were used to assess the respiratory status. A lack of confirmed improvement of lung volumes may extend the duration of ventilation, prolonged exposure to high FiO2, and high inspiratory pressure resulting in an increase of occurrence of pneumothorax, intraventricular haemorrhage, and related complications. Surfactant lung lavage together with surfactant administration improved the elastic properties of the lungs, what is reflected by an increase of compliance (C), and decrease of airway resistance, mean airways pressure, ventilatory settings and oxygenation index. Surfactant lung lavage followed by administration of surfactant probably stopping migration of meconium and did not allowed to spread an obstructive changes in small bronchioli and alveolar ducts.