Minimally Invasive Surfactant Therapy and Noninvasive Respiratory Support

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KEYWORDS

• Continuous positive airway pressure • Minimally invasive surfactant therapy
• Less invasive surfactant therapy • Respiratory distress syndrome • Preterm infant

KEY POINTS

- CPAP and mechanical ventilation with surfactant application are efficacious therapies of RDS.
- Use of noninvasive modes of respiratory support is recommended as primary therapy in RDS of premature infants.
- Several strategies of minimally invasive surfactant therapy (MIST) to combine the advantages of noninvasive respiratory support and of surfactant therapy have been reported.
- Available data suggest that these strategies may reduce the need for mechanical ventilation and improve outcome of preterm infants under certain conditions.
- Research is still needed to define the conditions for adequate use of MIST.

INTRODUCTION

Respiratory distress syndrome (RDS) caused by surfactant deficiency remains one of the major reasons of neonatal mortality and short- and long-term morbidity in preterm infants. Use of noninvasive modes of respiratory support and intubation, positive pressure ventilation, and surfactant therapy are efficacious therapies of RDS. Continuous positive airway pressure (CPAP) can only be used as primary respiratory support in infants who start spontaneous breathing after birth. When perinatal care of premature infants is optimized by using antenatal steroids and optimizing birth management most preterm infants start spontaneous breathing. In this setting recent studies demonstrate that outcome of preterm infants treated with CPAP alone is at least comparable with that of infants treated with intubation, positive pressure ventilation, and surfactant application.[1–3] Three meta-analyses suggest a superiority of CPAP

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regarding the outcome of bronchopulmonary dysplasia (BPD).[4–6] These findings led to the recommendation to use noninvasive modes as primary respiratory support in premature infants by the European Association of Perinatal Medicine and the American Academy of Pediatrics.[7,8]

Nevertheless surfactant, after its introduction at the end of the 1980s, has significantly improved outcome of premature infants. Therefore the combination of noninvasive modes of respiratory support with the administration of surfactant may combine two efficacious principles. The intubation surfactant extubation (INSURE) approach is a well-established strategy to combine both principles. A recent systematic review and meta-analysis pooled nine trials that compared early INSURE with CPAP alone in infants with RDS who had never before been intubated. This revealed no statistically significant differences between INSURE and CPAP alone for BPD and/or death, but the relative risk estimates seemed to favor INSURE.[9] As a consequence further adequately powered trials are needed.

However, although INSURE is well-established and seems to be beneficial it still needs at least a short period of positive pressure ventilation that could induce lung injury. Avoidance of any positive pressure ventilation combined with surfactant may have further benefits. Therefore, some strategies to combine noninvasive modes with surfactant therapy have been reported. These strategies are minimally invasive surfactant therapy or less invasive surfactant application.

DIFFERENT MODES OF MINIMALLY INVASIVE SURFACTANT THERAPY

In a metanarrative review More and coworkers[10] reported the different modes of minimally invasive surfactant therapy. These are surfactant application into the pharynx, surfactant nebulization, surfactant application via a laryngeal mask, and surfactant application via a thin endotracheal catheter. **Box 1** provides an overview of available human data for the different approaches.

Surfactant Application into the Pharynx

Surfactant application into the pharynx is the oldest approach that was tested in a randomized trial.[11] This approach is based on the idea that surfactant spreads at the fluid-air interface when the baby starts breathing. Infants with a gestational age of 27 to 29 weeks were included into the study. Surfactant was given immediately after birth, without noninvasive respiratory support. The study found a decrease in severity of RDS, less mechanical ventilation during the first 10 days, and a lower mortality (19% vs 30%) in the intervention group. However, the interpretation of the study is difficult because many infants also received surfactant via an endotracheal tube after intubation. Surprisingly the method was only evaluated in one further study, where surfactant was given into the nasopharynx immediately after birth of the shoulders.[12] In contrast to the first study in this trial the surfactant application was combined with postnatal respiratory support with CPAP. A total of 13 of 15 infants who were delivered vaginally were weaned quickly to room air, whereas five of eight infants who were delivered by caesarean section had to be intubated soon after birth. Because this approach is really minimally invasive, it warrants further investigation.

Surfactant Nebulization

Nebulization of surfactant is also an old idea. If efficacious it would be an attractive alternative to any other mode of application because it is really noninvasive. Any manipulation of the airways is avoided and the application is independent of the