Observational Study on Less Invasive Surfactant Administration (LISA) in Preterm Infants < 29 Weeks – Short and Long-term Outcomes

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Though early surfactant administration to very low birth weight infants needing mechanical ventilation decreases mortality and morbidity, there is an ongoing debate when to intubate these infants for surfactant administration. Several trials have not found convincing evidence that early surfactant administration after tracheal intubation is beneficial compared to stabilization of these infants by nasal continuous pressure ventilation and giving surfactant only to infants with CPAP failure.

A recent randomized controlled trial has demonstrated short-term benefits of a new minimally invasive procedure of surfactant administration in spontaneously breathing preterm infants ≥ 26 weeks (less invasive surfactant application, LISA) compared to the conventional route. With LISA surfactant can be given without mechanical ventilation. It is unknown, whether application of this method in preterm infants less than 26 weeks is effective and safe and whether this method can effectively be implemented on a NICU. We report on short- and long-term outcomes of preterm infants < 29 weeks GA before and after implementation of this method including infants 23 + 0 to 25 + 6 weeks of gestation.

**Patients and Methods:** Preterm infants born between 23 + 0 and 28 + 6 weeks gestational age born during two periods, 18 months before (n = 44) and after introduction of LISA (n = 53), were analyzed for neonatal outcomes. We were able to assess neurodevelopment by the Bayley Scales for Infant Development Inventory II in 52% of discharged infants at corrected age of 36 months.

**Results:** Perinatal risk factors were evenly distributed between both periods, mean birth weight was 903 g and mean gestational age was 26 + 1 completed weeks of gestation. Surfactant was given to 73% of infants in period 1 and 83% in period 2 (p = 0.22). In period 2 66% of the preterm infants needing surfactant received it by the new method, they needed fewer repetitive doses (17% vs 57%, p = 0.03) and received fewer bag-and-mask ventilation during delivery room stabilization (62% vs. 100%, p = 0.006). In period 2 fewer patient had to be ventilated during the first 3 days of life (42% vs 77%, p < 0.0005) and overall (55% vs. 77%, p = 0.02). The duration of mechanical ventilation was 2 vs 3 days (p = 0.056). Survival without BPD was 68% in period 1 and 74% in period 2 (p = 0.29). In period 2 fewer infants had a diagnosis of nosocomial sepsis (43% vs 66%, p = 0.04), use of systemic glucocorticoids declined (7.5% vs. 23%, p = 0.04) , more infants received doxapram (34% vs 2.3%, p < 0.0001). 48% of the infants having been treated with LISA had to be intubated during their NICU course mainly due to severe apneas. Other neonatal outcomes did not differ between both groups. At 36 months of corrected age the mental developmental index (MDI) rose between both periods from 89 to 98 (p = 0.16), the physical developmental index (PDI) from 83 to 91 (p = 0.03) (see figure 1). Severe impairment occurred in 29% of infants of period 1 and 23% of infants in period 2.

**Discussion:** Implementation of the LISA method on our neonatal ward was feasible and was not associated with worse neurological outcomes. It was associated with less need for mechanical ventilation in infants > 24 weeks of gestation compared to a historical control group. Due to the retrospective non-randomized nature of our study and the high-drop-out rate during follow-up the observed trends for better pulmonary and neurocognitive outcomes warrant further follow-up studies of ongoing or recently finished randomized trials on this new method.

![Fig. 1](image-url) Box plots of MDI and PDI at 36 months corrected age in both periods.

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