A randomised control study of partial liquid ventilation after airway lavage with exogenous surfactant in a meconium aspiration syndrome animal model

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Abstract

**Aims**—To test the hypothesis that lavage with exogenous surfactant before partial liquid ventilation in meconium aspiration syndrome (MAS) would improve debris removal, and therefore the effectiveness of partial liquid ventilation.

**Methods**—12 newborn piglets were randomised into 4 groups, partial liquid ventilation or gas ventilation, with and without surfactant lavage. Physiological and blood gas data were compared between groups by analysis of variance.

**Results**—Arterial oxygen pressure (PaO₂) was improved in the group treated with surfactant lavage when compared with the group not receiving surfactant. PaO₂ in the group receiving surfactant lavage followed by partial liquid ventilation was further improved when compared with the group treated with surfactant lavage followed by gas ventilation and the group receiving partial liquid ventilation alone.

**Conclusion**—The effectiveness of partial liquid ventilation in MAS might be enhanced by pretreatment with exogenous surfactant bronchial lavage.

(Keywords: meconium aspiration syndrome; partial liquid ventilation; exogenous surfactant)

Meconium aspiration syndrome (MAS) is a common cause of lung disease in neonates. Despite recent advances in neonatal respiratory care, infants with MAS continue to be candidates for extracorporeal membrane oxygenation, inhaled nitric oxide, and high pressure limited ventilation. Liquid associated ventilation is a necessary to achieve a PaO₂ value lower than 8 kPa. Repeat doses of meconium were administered as necessary to achieve a PaO₂ value lower than 8 kPa at 15 minutes after meconium instillation. The mean total amount of 20% human meconium slurry was 6.5 ml; there was no significant difference between groups. Animals were mechanically ventilated for one hour after meconium instillation to produce the lung injury model. This lung model has been used...
Effect of exogenous surfactant in an animal MAS model

Figure 2 shows the PaCO2 values. After higher than the other groups at 30 minutes (liquid ventilation) remained significantly carbon dioxide pressure (PaCO2) was over 12 kPa, were excluded from the study because they did not comply with the MAS model, and the remaining 12 piglets were randomised into two groups as surfactant lavage group or suction group.

The surfactant lavage group (n = 6) received four aliquots of 12 mg/kg of exogenous surfactant (surfactant-TA; Tokyo Tanabe, Tokyo, Japan) diluted in 2.5 ml normal saline instilled into four different positions to promote distribution. Gentle manual ventilation was performed after each instillation, followed by repeated bronchial suctioning by means of a 6.5 gauge French suction catheter.

The suction group (n = 6) received tracheal suctioning with a 6.5 gauge French suction catheter until the suctioned fluid was clear.

Thirty minutes after bronchial lavage with exogenous surfactant or suction, blood gas sampling was performed, and then the animals were randomised to four groups as follows.

Group 1 (surfactant + partial liquid ventilation; n = 3). Preoxygenated PFC (Fluorinart 84; 3M Group, Osaka, Japan) was administered via the pressure monitoring port of the endotracheal tube over one to two minutes in an amount that approximated the animal's functional residual capacity, which was estimated by the visible meniscus of PFC in the endotracheal tube. The meniscus should be checked with no positive end expiratory pressure. Fluorinart is a PFC with a specific gravity of 1.73 g/cm3 at 25°C, surface tension of 13.0 dyne/cm, vapour pressure of 10.5 kPa at 37°C, and an O2 solubility of 59 ml/100 ml and CO2 solubility of 224 ml/100 ml at 37°C at one atmosphere of pressure.

Group 2 (surfactant + gas ventilation; n = 3). Animals were maintained after surfactant lavage at the same ventilator setting throughout the study.

Group 3 (suction + partial liquid ventilation; n = 3) received PFC as group 1 after bronchial suction.

Group 4 (suction + gas ventilation; n = 3) received no PFC and bronchial suction.

**STATISTICAL ANALYSIS**

Physiological parameters were expressed as mean (SEM) and were compared using analysis of variance (ANOVA) for repeated measures with Fisher’s tests. A significant difference was set at p < 0.05.

**Results**

Figure 1 shows changes in PaO2 over time. After bronchial lavage with surfactant, PaO2 was significantly greater than in those animals that had not been treated with surfactant. In addition, PaO2 in group 1 (surfactant + partial liquid ventilation) remained significantly higher than the other groups at 30 minutes after the initiation of partial liquid ventilation. Figure 2 shows the PaCO2 values. After bronchial lavage with surfactant, PaCO2 tended to decrease compared with the group that did not receive surfactant, although the difference was not significant. After the initiation of partial liquid ventilation, group 1 (surfactant + partial liquid ventilation) had significantly lower PaCO2 values than group 4 (suction + gas ventilation).

**Discussion**

The lung pathophysiology associated with MAS in the newborn infant includes airway obstruction, impaired gas diffusion, pulmonary vascular hypertenstion, and pulmonary inflammation. To achieve effective meconium debris removal without inactivating or washing out surfactant, a bronchial lavage with exogenous surfactant has been proposed. In addition, total liquid ventilation with PFC might also remove meconium debris, without removing surfactant. In a meconium strained lamb model, Fousta and others reported that total
liquid ventilation with PFC improved alveolar recruitment and improved compliance when compared with control gas ventilated animals. In addition, the lung histology of the total liquid ventilation group demonstrated clear, intact alveolar epithelium and homogeneously expanded alveoli, whereas non-homogeneous aeration of alveoli and partial atelectasis was seen in the partial liquid ventilation group. We speculated that PFC in partial liquid ventilation would not be as effective as saline or surfactant at debris removal and partial liquid ventilation after surfactant lavage would optimise the effectiveness of partial liquid ventilation in the MAS model.

In our study, we evaluated the effectiveness of a combined surfactant lavage with partial liquid ventilation in a piglet model of MAS. When the animals were treated with exogenous surfactant lavage after injury but preceding partial liquid ventilation, improvement in gas exchange was observed. In contrast, without previous surfactant lavage, these improvements were not seen after partial liquid ventilation. These results suggest that pretreatment of infants with MAS with a surfactant lavage might improve the efficacy of partial liquid ventilation by optimising debris removal and improving the distribution of ventilation during partial liquid ventilation. The use of a combined exogenous surfactant and partial liquid ventilation has also been shown to be effective in a surfactant deficient animal model. In this model, exogenous surfactant might improve spreading and uniform distribution of the PFC by reducing surface tension at the alveolar surface before the initiation of partial liquid ventilation. This mechanism might, in fact, also be present in the MAS model used in our study.

Therefore, our results suggest that improvement in lung function with partial liquid ventilation in MAS might be enhanced by pretreatment with exogenous surfactant bronchial lavage.

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