Short Communication

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The Effects of Surfactant on Oxygenation in Term Infants with Respiratory Failure

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Abstract

Objective: The objective of the study was to evaluate the effects of exogenous surfactant on respiratory indices in term infants with respiratory failure.

Methods: Consecutive 18 mechanically ventilated term infants, who received a single dose of exogenous surfactant were retrospectively included into the study. The respiratory outcome of surfactant rescue therapy was evaluated by comparing respiratory indices before and six hours after surfactant administration.

Findings: Median oxygenation index (OI), mean alveolar pressure (MAP) and fraction of inspired oxygen (FiO_2) values were significantly decreased (P<0.001); median arterial oxygen partial pressure (PaO_2), arterial oxygen saturation (SaO_2) and PaO_2/FiO_2 values were significantly increased six hours after surfactant treatment (P<0.001).

Conclusion: Rescue therapy with surfactant was found to be effective in the improvement of early respiratory indices in term infants with respiratory failure.

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Key Words: Surfactant; Infant; Pneumonia; Oxygenation; Respiratory Failure; Neonate

Introduction

Surfactant has become standard therapy in preterm infants with respiratory distress syndrome (RDS)[1]. Surfactant lowers the alveolar surface tension and prevents expiratory alveolar collapse increasing compliance, reducing pulmonary vascular resistance and improving ventilation-perfusion mismatching. Surfactant can be inactivated in term infants with pneumonia, meconium aspiration syndrome, lung hypoplasia and pulmonary hemorrhage. This inactivation may be caused by various plasma proteins and local inflammatory cytokines that pass into the airways, damage type II pneumocytes and alveolar cells rendered vulnerable by mechanical ventilation. Case reports and studies from literature suggest that surfactant might be beneficial to infants with sepsis and pneumonia[2].

This study aimed to evaluate the effects of exogenous surfactant on ventilation parameters and oxygenation of term infants with respiratory failure.

Subjects and Methods

This is a case series study in which mechanically ventilated infants diagnosed with early neonatal sepsis and respiratory failure that

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had received a single dose of exogenous bovine surfactant (Survanta®) between January 2008 and December 2010, with a gestational age above 37 weeks were retrospectively studied. Diagnoses like meconium aspiration syndrome, persistent pulmonary hypertension of the newborn, asphyxia, and pulmonary hemorrhage were excluded. All infants suffered from severe respiratory failure according to definition of the European-American consensus conference with arterial oxygen partial pressure (mmHg) (PaO_2)/ fraction of inspired oxygen (FiO_2) below 200 mmHg[3]. Diagnosis was confirmed with antenatal history, clinical, radiological and laboratory findings. Because signs of sepsis are nonspecific, any term newborn infant with sudden onset of respiratory distress or other signs of illness was evaluated for sepsis including complete blood count, blood smear, C-reactive protein, blood cultures and tracheal aspirates. Mothers were also screened for Group B streptococcal (GBS) infection. Surfactant was given as rescue treatment when mechanical ventilation had failed to improve oxygenation. All infants were followed with synchronized intermittent mandatory ventilation (SIMV) mode of ventilator (SLE 2000®). Ventilator settings were adjusted with arterial blood gas results.

Early outcomes of surfactant treatment were evaluated via respiratory indices including oxygenation index (OI), mean alveolar pressure (MAP), FiO_2, PaO_2, arterial oxygen saturation (SaO_2) and PaO_2/FiO_2 values. These values were carried out using arterial blood gas values and ventilator parameters of the infants before and six hours after surfactant administration.

OI and MAP were calculated using the following equation:

$$OI=(MAP \times FiO_2 \times 100)/ PaO_2$$

$$MAP=[(PIPxTI)+(PEEPxTE)]/TI+TE$$

PIP: peak inspiratory pressure (cmH_20)
TI: time of inspiration (sec)
PEEP: positive end expiratory pressure (cmH2O)
TE: time of expiration (sec)

Comparisons between groups were done with Wilcoxon Signed Ranks Test and Mann-Whitney U Test. $P<0.05$ was considered to be significant.

Findings

Mean gestational age of the infants was 38.3±1 weeks, mean birth weight was 3088 grams and median hospitalization day was 1 day (Table 1). Although GBS screening was negative in all mothers, eight mothers had clinical or histological chorioamnionitis, seven had prolonged ruptured membranes (>24 hours) and three had fever (>38.3˚C) before labor. All infants had leucocytosis (16502±6704/mm^3), elevated CRP (33.0±3.4 mg/L), and bilateral alveolar densities with air bronchograms on chest x-rays; however, tracheal and blood cultures were negative in all patients so that patients were diagnosed as suspected sepsis.

In all of the 18 infants pulmonary gas exchange was critically impaired with median PaO_2/FiO_2 below 100 mmHg prior to surfactant administration. All patients received a single dose (total phospholipid dose 100mg/kg) surfactant when mechanical ventilation failed to improve oxygenation. Of these infants, one suffered from pneumothorax within 24 hours after surfactant administration and two infants died due to multiorgan failure within the first week postpartum.

Before the surfactant treatment, median (minimum and maximum) OI, MAP, FiO_2, PaO_2, SaO_2 and PaO_2/FiO_2 values were as follows; 15.3 (10.0-52.8); 8.5 (7.0-15.0); 80.0 (50.0-100.0); 45.4 (21.5-56.9); 83.5 (42.0-97.0); 60.3 (21.5-99.2). Ventilator settings were adjusted with arterial blood gas results. Following surfactant treatment these values were; 3.4 (1.5-35.0); 8.0 (6.0-14.0); 40.0 (21.0-100.0); 83.5 (39.0-118.0); 97.0 (50.0-

Table 1: Demographic characteristics of infants

Variable	Description
Birth weight (g)*	3.088 (401)
Male/Female	22.6
Mode of birth (Vaginal/ cesarean section)	3.25
Initial hospitalization day†	1.0 (1.0-4.0)

* Mean±standard deviation ; †Median (minimum, maximum)

Table 2: Respiratory indices of patients before and after surfactant treatment[1]

Parameter	Before surfactant treatment	After surfactant treatment	*P.* value
Oxygenation index	15.3 (10.0-52.8)	3.4 (1.5-35.0)	<0.001
Mean alveolar pressure	8.5 (7.0-15.0)	8.0 (6.0-14.0)	0.002
Fraction of inspired oxygen (FiO_2)	80.0 (50.0-100.0)	40.0 (21.0-100.0)	0.001
Arterial oxygen partial pressure (PaO_2)	45.4 (21.5-56.9)	83.5 (39.0-118.0)	<0.001
Arterial oxygen saturation SaO_2	83.5 (42.0-97.0)	97.0 (50.0-99.5)	<0.001
PaO_2/FiO_2	60.3 (21.5-99.2)	234.0 (39.0-422.0)	<0.001

[1]Median (minimum-maximum)

99.5); 234.0 (39.0-422.0) respectively. OI, MAP and FiO_2 values significantly decreased. Whereas PaO_2, SaO_2 and PaO_2/FiO_2 values significantly increased (P<0,001). Values are shown in Table 2.

Discussion

Preterm and late preterm infants have increased risk of RDS so that surfactant treatment guidelines mostly focuses on these group of patients[4]. Term infants are also at risk of RDS and any lung disease affecting these infants that involves surfactant dysfuncion or deficiency constitutes a potential target for replacement therapy. Anadkat et al, have demonstrated that male sex and white race ethnicity increase the risk of RDS in late preterm and term infants[5]. Surfactant treatment response starts with improvement in PO_2 as also shown in our study, followed by improvement in compliance and oxygenation a more prolonged effect over hours that we evaluated by OI, then finally prolonged effect of the surfactant as substrate for surfactant metabolism persisting for weeks[6].

Preterm infants diagnosed with RDS that have not responded to surfactant treatment as expected have been found to suffer from a significantly higher rate of infection and birth asphyxia[7]. It is also known that surfactant plays an important role against pulmonary infections. Pneumonia in term infants might result in secondary surfactant deficiency or dysfunction as surfactant can be inactivated. Secondary surfactant deficiency can result in respiratory deterioration and this may potentially affect the severity of illness in infants with pneumonia. These infants might also need ventilatory support or extracorporeal membrane oxygenation (ECMO) during their hospitalization. If an infant is intubated and exhibits a deteriorating condition during this ventilatory support, exogenous surfactant may improve infant's respiratory status because surfactant can be easily inactivated by the inflammatory products of lung injury caused by mechanical ventilation, supplemental oxygen or infection[8]. In a multi-center trial it was shown that surfactant treatment of term infants with severe respiratory failure also can decrease the need for ECMO[9]. In this study infants were randomized to receive exogenous surfactant or placebo. The infants responded to surfactant better if the surfactant had been given at the early stages of respiratory failure evaluated by OI. In our study it is also shown that surfactant treatment rapidly improved gas exchange and oxygenation in infants with respiratory failure. Surfactant has important antimicrobial properties and since endogenous surfactant can potentially be inactivated by inflammation and edema in pneumonia patients, exogenous surfactant may be useful in the treatment. Herting et al, studied the effects of surfactant on 8 children diagnosed with acute respiratory distress triggered with pneumonia and found that PaO_2/FiO_2 was immediately increased after surfactant instillation[10]. It is also shown that surfactant therapy improves gas exchange in the majority of infants with streptococcal pneumonia but response was found to be slower compared with infants with RDS[11]. Referring to this study Jobe concluded that there should be no concerns about treating infants with sepsis/pneumonia syndromes and respiratory failure with surfactant[12]. In our study we also demonstrated that infants presenting with respiratory failure

and early neonatal sepsis benefit from surfactant administration in the early hours of treatment.

There are some limitations to our study. First this was a retrospective study; second, there was no control group; thus there may have been confounding factors which contributed to the outcome. Although, there is still no consensus on the efficacy of surfactant in infants with suspected or proven pneumonia[13], this study shows that surfactant treatment can improve respiratory indices in infants diagnosed with early neonatal sepsis and respiratory failure. However larger randomized controlled trials are necessary to determine and conclude whether improved oxygenation is due to surfactant.

Conclusion

Exogenous surfactant improves respiratory indices in infants with respiratory failure.

Acknowledgment

This study was approved by our local ethic committee.

Conflict of Interest: None

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