Original Research Article

A study of role of surfactant therapy in patients of meconium aspirations at a tertiary health care center

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Abstract

Background: MAS is defined as respiratory distress in a neonate born through meconium-stained amniotic fluid (MSAF) with characteristic radiological findings (hyperinflation and patchy opacities) whose symptoms cannot be explained otherwise. Use of surfactant is also recommended for treatment of MAS. Surfactant is administered intratracheally as either a bolus dose or in dilute form to lavage the lungs in neonates with MAS. In this study, we evaluated role of surfactant therapy in patients of meconium aspirations at our tertiary health care center. **Material and Methods:** This was a prospective, observational study carried out in neonates with evidence of meconium aspiration syndrome such as presence of meconium stained amniotic fluid or staining of meconium in skin, umbilical cord or nails, presence of meconium below vocal cords and Chest x-ray suggestive of meconium aspiration. **Results:** In present study 30 cases were included satisfying inclusion and exclusion criteria. In study 18 male and 12 female babies were included. 19 babies were term while 11 babies were pre-term. 21 babies were Appropriate for Gestational Age and 9 babies were small for Gestational Age. Mean gestational age was 37.2 ±1.6 weeks. Mean birthweight was 2190 ± 280 grams. 22 babies were vaginally delivered, 8 delivered by LSCS. Intrapartum 17 babies had fetal heart rate abnormalities. 4 babies needed Chest compressions , 2 needed epinephrine during resuscitation. 2 babies received intubated and on PPV in NICU and 3 babies needed positive pressure ventilation (PPV) at birth,. APGAR scores at 1 min, 5 min and 10 minutes are noted. Average maximum respiratory distress score was 6 ±1.6. 21 babies needed mechanical ventilation. Average duration of mechanical ventilation was 18.5 ± 43.8 hours while average duration of CPAP was 26.4 ± 19.3 hours. 11 ± 8.5 days was average duration of hospital stay. We noted Sepsis, Pneumothorax. PPHN in 4,1 and 1 cases respectively. 22 babies were discharged uneventfully. We noted mortality in 8 cases. **Conclusion:** Meconium aspiration syndrome is a serious and potentially preventable condition . Surfactant therapy in MAS can reduce the severity of respiratory illness and progressive respiratory failure when used early and judiciously in infants with severe respiratory distress.

Key Words: meconium aspiration syndrome, respiratory distress syndrome, surfactant,

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INTRODUCTION

Meconium is a sterile, odorless, blackish green material comprising intestinal and pancreatic secretions, desquamated cells, vernix caseosa, lanugo hair, bile pigments, amniotic fluid, and blood. Under normal circumstances, passage of meconium from the fetus into amnion is prevented by the lack of intestinal peristalsis due to low motilin levels, tonic contraction of anal sphincter, and a terminal cap of viscous meconium[1]. Apart from fetal maturation, various fetomaternal stress factors like maternal hypertension, oligohydramnios, maternal drug abuse (especially tobacco and cocaine), primigravidity, anemia, chorioamnionitis, prolonged

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labor, fetal distress, cord problems, and fetal growth retardation promote passage of meconium.[2]Meconium aspiration syndrome (MAS) is a result of ante- or postpartum aspiration of meconium-stained amniotic fluid in term or near-term infants resulting in respiratory morbidity of varying severity. MAS is defined as respiratory distress in a neonate born through meconium-stained amniotic fluid (MSAF) with characteristic radiological findings (hyperinflation and patchy opacities) whose symptoms cannot be explained otherwise.[3]Interventions such as elective reduction of post-term births, aggressive management of fetal distress, amnioinfusion and reduced incidence of birth asphyxia have resulted in a significant decline in MAS incidence4. Excellent NICU setups, advent of newer therapies like inhaled NO, surfactant, high-frequency ventilation and extracorporeal membrane oxygenation (ECMO) has resulted in tremendous improvements in MAS survival. Use of surfactant is also recommended for treatment of MAS. Surfactant is administered intratracheally as either a bolus dose or in dilute form to lavage the lungs in neonates with MAS. Although bolus administration is thought to replenish the endogenous surfactant inactivated by fatty acids present in the meconium, lung lavage with surfactant is believed to wash the residual meconium from the airways.[5] In this study, we evaluated role of surfactant therapy in patients of meconium aspirations at our tertiary health care center.

MATERIAL AND METHODS

This was a prospective, observational study carried out in neonatal intensive care unit, under department of paediatrics, XXX medical college and Hospital, XXXX. Study period was from January 2019 till October 2019. Institutional ethical committee approval was taken. Study was conducted in neonates with evidence of meconium aspiration syndrome such as presence of meconium stained amniotic fluid or staining of meconium in skin, umbilical cord or nails, presence of meconium below vocal cords and Chest x-ray suggestive of meconium aspiration.

Inclusion Criteria

1. Gestation age ≥ 34 weeks
2. Presence of respiratory distress (Downe's score ≥4) within 2 hours of birth.
3. Need for mechanical ventilation within 6 h of birth
4. Parents willing for follow up of babies after discharge

(* - Downe score is an objective method to assess the severity of respiratory distress in newborns. It includes respiratory rate (RR), recessions, grunt, air entry and fractional oxygen requirement. Each parameter is score on a scale of 0, 1 and 2 with increasing severity. Total score ranges from 0 to 10.)

Exclusion Criteria

1. Neonates who had major congenital malformations, antenatally diagnosed congenital heart disease, hydrops fetalis
2. Babies with pneumothorax, pulmonary hemorrhage and hemodynamic instability with mean blood pressure <40 mmHg and oxygen saturation <90% at randomization
3. Babies taken discharge against medical advice after inclusion in study

A written informed consent was taken from parents/guardians. Either Survanta at 4 ml/kg (150 mg/kg) or Neosurf at 5 ml/kg (135 mg/kg) were given, depending on the availability. Intratracheal bolus administration of surfactant was given. Timing of administration of surfactant was either as early rescue (administration of surfactant within 2 hours of birth) or late rescue (administration after 2 hours of birth). Only cases with early rescue were included. Routine neonatal care was provided. Repeat doses were given to babies requiring FiO2 of more than 35% and mean airway pressure of more than 7 cm H2O to maintain a PO2 of 50-70 mmHg[9]. During the course of NICU stay duration of respiratory support, need for mechanical ventilation, severity of respiratory distress (Downe score), duration of mechanical ventilation, duration of oxygen therapy, duration of hospitalization and incidences of air leak, persistent pulmonary hypertension of the newborn (PPHN) and infection, mortality were recorded in case proforma and analysed. Follow up was kept till neonatal period.

RESULTS

In present study 30 cases were included satisfying inclusion and exclusion criteria. In study 18 male and 12 female babies were included. 19 babies were term while 11 babies were pre-term. 21 babies were Appropriate for Gestational Age and 9 babies were small for Gestational Age. Mean gestational age was 37.2 ±1.6 weeks. Mean birthweight was 2190 ± 280 grams. 22 babies were vaginally delivered, 8 delivered by LSCS. Intrapartum 17 babies had fetal heart rate abnormalities. 4 babies needed Chest compressions, 2 needed epinephrine during resuscitation. 2 babies received intubated and on PPV in NICU and 3 babies needed positive pressure ventilation (PPV) at birth. APGAR scores at 1 min, 5 min and 10 minutes are noted.

Table 1: Demographic data

Characteristics	Value
Male/Female (n)	18/12
Term/Late preterm (n)	19/11
*AGA/SGA (n)	21/9
Gestational age (wk)	37.2 ±1.6 weeks
Birthweight (g)	2190 ± 280 grams
Mode of delivery - Vaginal/Emergency lower segment cesarean section	22/8
Fetal heart rate abnormalities	17
Need for positive pressure ventilation (PPV) at birth	3
Chest compressions	4
Received intubated and on PPV in NICU	2
Need for epinephrine	2
APGAR score 1 min (>7/4-7/<4)	2/17/11
APGAR score 5 min (>7/4-7/<4)	0/16/14
APGAR score 10 min (>7/4-7/<4)	0/16/14

***AGA-Appropriate for Gestational Age, SGA-Small for Gestational Age**

Average maximum respiratory distress score was 6 ±1.6. 21 babies needed mechanical ventilation. Average duration of mechanical ventilation was 18.5 ± 43.8 hours while average duration of CPAP was 26.4 ± 19.3 hours. 11 ± 8.5 days was average duration of hospital stay. We noted Sepsis, Pneumothorax. PPHN in 4,1 and 1 cases respectively. 22 babies were discharged uneventfully. We noted mortality in 8 cases.

Table 2: Treatment outcome measures

Outcome	Value
Maximum respiratory distress score	6 ±1.6
Use of mechanical ventilation	21
Duration of mechanical ventilation	18.5 ± 43.8 hours
Duration of CPAP	26.4 ± 19.3 hours
Duration of hospital stay	11 ± 8.5 days
Complications	
Sepsis	4
Pneumothorax	1
PPHN	1
Outcome	
Discharge	22
Death	8

DISCUSSION

Intrapartum passage of meconium is a common problem seen in the delivery room, followed by admission of newborn to newborn care units. Meconium aspiration syndrome (MAS) is an important cause of respiratory distress in neonates, sometimes leading to respiratory failure and even death. Fetal passage of meconium leading to MSAF complicates about 7%–20% of all pregnancies worldwide[6]. The incidence also increases as the gestational age advances with reported frequencies at 37, 40, and >42 weeks being 3%, 13%, and 18% respectively[7]. Despite substantial research, the pathophysiology of MAS is complex and still incompletely clarified. Aspiration of meconium interferes with normal respiratory physiology by causing airway obstruction, chemical irritation, inflammation, surfactant inactivation, meconium induced apoptosis and there is increased risk to develop air leaks, Persistent Pulmonary Hypertension of newborn (PPHN) and sepsis. [8,9] Respiratory distress with marked tachypnea, retractions, grunting, nasal flaring, and cyanosis ensues soon after birth. Affected infants typically have a barrel-shaped chest with an increased anterior-posterior diameter caused by overinflation. Chest auscultation reveals rales and rhonchi. Some other approaches to prevent or treat MAS include amnioinfusion (infusion of saline into the amniotic cavity), oronasopharyngeal suctioning of meconium-stained neonates before delivery. Prophylactic intrapartum amnioinfusion for moderate or thick MSAF was thought to reduce the frequency of MAS, cesarean section rate, meconium below the vocal cords, and neonatal acidemia. But this intervention can cause potential complications such as chorioamnionitis, premature rupture of membranes, placental abruption, preterm labor, cord hemorrhage, cord prolapse, amniotic fluid embolism, and maternal death.[10] However a

Cochrane meta-analysis review suggests amnioinfusion to be considered for women with meconium-stained liquor in units with limited facilities for peripartum surveillance, and with no demonstrable reduction in MAS incidence in settings with standard peripartum surveillance.[11] With the recognition of role of chronic in utero hypoxia and associated perinatal asphyxia in pathogenesis of MAS, routine endotracheal suctioning is no longer recommended even in nonvigorous infants with MAS. [12] The decreased mortality rates of newborn babies with MAS from 40% to 25% in recent studies[13,14]; is directly related to change in obstetric qualifications and use of respiratory supports as exogenous surfactant, nitric oxide and high frequency ventilation. The detrimental effect of meconium on surfactant production and function has been well known and forms the basis of the use of exogenous surfactant in severe MAS. Meconium components (cholesterol and bile acids) inactivate lung surfactant by changing the viscosity and ultrastructure of surfactant, fragmentation of dipalmitoylphosphatidylcholine and accelerating its conversion from large, surface-active aggregates into small, less active forms. It also decreases the levels of surfactant proteins A and B and directly harms type II pneumocytes, thereby decreasing surfactant production.[15] In recent clinical trials, improved gas exchange following surfactant treatment was demonstrated in both term and preterm neonates with respiratory conditions other than surfactant deficient RDS, such as meconium aspiration syndrome, bacterial pneumonia and bronchopulmonary dysplasia.[16] Surfactant therapy in MAS is analysed by various researchers. A meta-analysis of four trials (*n*=326), surfactant replacement by bolus or slow infusion in infants with severe MAS had no statistically significant effect on mortality [typical risk ratio (RR) 0.98, 95% CI 0.41 to 2.39].[16] Another meta-analysis incorporated eight RCTs of surfactant for MAS with a total of 512 patients, reported that surfactant significantly treatment reduced oxygenation index, increased arterial oxygen/alveolar oxygen ratio, shortened hospitalization days and decreased mortality rate. There was no statistical difference in the durations of mechanical ventilation and oxygen therapy, and the incidences of air leaks, pulmonary hemorrhage and intracranial haemorrhage between the two groups[17]. In a meta-analysis of surfactant lavage, lung lavage with diluted surfactant was shown to be beneficial to infants with MAS in terms of reduction in composite outcome of death or use of ECMO (RR 0.33, 95% CI 0.11 to 0.96; *n*=88).[18] Clinical trials of surfactant lung lavage have suggested that lavage therapy may improve oxygenation and shorten the duration of ventilation. [19] However, a meta-analysis of two RCTS did not show any significant improvement in mortality, pneumothorax, duration of ventilation, or duration of hospitalization.[18] In another RCT, authors demonstrated no effect of lavage on pulmonary outcomes but found a higher rate of ECMO free survival in the treated group. [20] A recent systematic review evaluating the effect of surfactant administration either as bolus or lavage concluded that both decreased the duration of hospital stay, the duration of mechanical ventilation, and the need for ECMO with no reduction in mortality[21]. Though we have not compared with control group but our findings are in accordance with this systematic review. Cochrane review concluded that in infants with MAS, surfactant administration may reduce the severity of respiratory illness and decrease the number of infants with progressive respiratory failure requiring support with ECMO. The relative efficacy of surfactant therapy compared to, or in conjunction with, other approaches to treatment including inhaled nitric oxide, liquid ventilation, surfactant lavage and high frequency ventilation remains to be tested. [16] The surfactant deficiency seen in MAS is not from an insufficient quantity of surfactant unlike a preterm neonate, but is likely a result of inhibited surfactant function(s) or alterations in surfactant composition. So, surfactant therapy should be used judiciously in MAS choosing infants with severe disease and treating early and if necessary, repeatedly, for optimum results. Further trials are needed to confirm the treatment effect, define the optimal doses and method of surfactant administration, and compare lavage with bolus administration.

CONCLUSION

Meconium aspiration syndrome is a serious and potentially preventable condition . Surfactant therapy in MAS can reduce the severity of respiratory illness and progressive respiratory failure when used early and judiciously in infants with severe respiratory distress.

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