Original Article

A comparative study of surfactant versus nonsurfactant therapy among preterm with respiratory distress syndrome

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ABSTRACT

Background: Respiratory distress is a clinical condition characterized by the presence of one or more signs of increased work of breathing including tachypnea, nasal flaring, grunting, and chest wall retraction. **Objective:** The objective of the study was to study the outcome of surfactant therapy in preterm with respiratory distress syndrome (RDS). **Materials and Methods:** A prospective comparative study was conducted in the neonatal intensive care unit of a tertiary care hospital in Cuttack, Odisha, over a period of 2 years. Parents of the babies, who gave their consent for surfactant (who can afford), were assigned as surfactant group while those who could not afford it, were included in nonsurfactant group after matching general characteristics. **Results:** Overall, mortality was less in the surfactant group (28.94%) than in nonsurfactant group (54.92%). However, the late neonatal death was more in the surfactant group (63.63%) than in nonsurfactant group (53.84%). Sepsis was the most common cause of the death in both groups, contributing 58% to overall death of both groups. **Conclusion:** Surfactant should be used in preterm with established RDS with due care to neonatal sepsis.

Key words: *Neonatal death, Preterm, Respiratory distress syndrome, Sepsis, Surfactant*

Every newborn carries immense possibility to transform into a complete healthy human being and fulfill the needs the future will demand. Of the newly born babies in our country 10–12% are born before 37 completed weeks are called premature, compared to 5–7% in the western country [1]. Live-born infant delivered before 37 weeks from the 1st day of last menstrual period are termed as “premature” by the WHO [2]. Low birth weight (LBW, birth weight of 2500 g or less) can be due to prematurity and intrauterine growth retardation or both. Approximately 57% of cases, under the age of 5, mortality occurs in a neonatal period of which 36% are attributable to prematurity [2,3].

With the evolution of neonatology, better understanding of neonatal physiology and advanced care, the intact neurobehavioral development survival of these newborn babies; especially, those <1000 g has increased to >90% [1]. Of the problems of a premature baby, respiratory causes are the most common cause of the admission to neonatal intensive care unit (NICU). The common respiratory problem is respiratory distress syndrome (RDS) or hyaline membrane disease (HMD), whose incidence increases as babies are born early [4-7]. It affects 60–80% of babies born before 28 weeks, 50% born between 28 and 32 weeks, 15–30% born between 32 and 36 weeks, and 10% born between 33 and 34 weeks [4-7]. RDS is an acute illness of preterm infant manifesting usually within 6 h characterized clinically by at 2 of the 3 essential features (NNF India) [8], i.e., (1) tachypnea (respiratory rate [RR] >60/min), (2) retractions (Intercostals and Subcostal), and (3) expiratory grunt. Downes score (term babies) and Silverman-Andersons scores (preterm babies) were used to assess the severity of RDS.

Prematurity is the most common etiological factor of RDS, and it is primarily due to the inadequate pulmonary surfactants with resultant diffuse alveolar atelectasis, edema, and cell injury. Prenatal diagnosis to identify the infant at risk, prevention of the disease by antenatal steroids, improved neonatal care, advances in respiratory support, and surfactant replacement therapy (SRT) have dramatically reduced mortality from RDS. Systematic reviews of RCT confirmed that SRT reduces initial inspired oxygen and ventilation requirements as well as incidence of severe RDS, death, pneumothorax, and other morbidity of prematurity [9-13]. However, RDS is still an important cause of morbidity and mortality in immature infants [14]. The objective of this study was to observe the outcome of surfactant therapy for RDS among preterm newborns.

MATERIALS AND METHODS

The study was conducted in the NICU of a tertiary care unit, in the department of pediatrics, Cuttack, from September 2010 to September 2012. Case selection was same in both the groups’, i.e., premature baby (<34 weeks) admitted in NICU with clinical signs and symptoms of RDS with X-ray features suggestive of RDS, after eliminating other possible differential diagnosis of respiratory distress. Cases were defined as respiratory distress in a premature baby with any 2 of 3 essential features, i.e., tachypnea (RR >60/min), retractions (intercostals and subcostal), and expiratory grunt. Newborns >34 weeks of gestation or birth weight ≥2000 g, or newborns having respiratory distress due to other causes such as surgical, metabolic causes, congenital respiratory tract anomaly, birth asphyxia, congenital heart disease, meconium aspiration syndrome, and infections including congenital pneumonia were excluded from the study. The parents who left against medical advice were also omitted from observation in both groups.

Parents were counseled about the role of SRT in addition to other supportive management. The need for the SRT and mechanical ventilation was decided in the presence of the following; Fio2 >0.35% to maintain Pao2 normal (60–80 mm-Hg) or Sp02 (88–93%) or having arterial/alveolar oxygen tension ratio (PaO_2/PAO_2 or a/A ratio <0.22). Babies, whose parents gave consent for the surfactant (and who can afford), were assigned as surfactant group while those, who could not afford it, were included in nonsurfactant group after matching the general characteristics. Written consent of the parents or legal guardians was taken in after explaining about the SRT. The adequate amount of surfactant was given to the babies while closely monitoring for the vital signs.

Antenatal history focusing history of premature rupture of membrane, history of previous pregnancy, doses of antenatal steroids, and causes for premature birth were recorded in a predesigned pro forma. Significant postnatal events and clinical examination findings with gestational age assessment by New Ballard scoring were also noted down. All babies in either group were started with fluids as per the weight and day of life, broad-spectrum antibiotic (ampicillin and gentamycin) with other supportive therapy on the individual and clinical basis. Routine and special investigations were sent on the individual clinical basis. In addition, pre-surfactant blood gas analysis and chest X-ray were also done.

Surfactant was administered after intubating and confirming the position ET tube clinically, and airway secretion was cleared. Surfactant was given in 2–3 aliquots with a baby in supine position. The patients were manually ventilated after each aliquot and simultaneously assessing for adequacy of airway, breathing, auscultation, Spo2, chest rise, heart rate, RR, blood pressure, pulse, and air entry and were put back on bubble-CPAP or mechanical ventilator depending on the clinical condition. No suctioning was done unless needed and for minimum 1 h.

Regular monitoring was done for vital signs, requirement of oxygen, ventilation settings at 30 min, 1, 6, 12, 24, 36 h, 48 h, and 72 h. Blood gas analysis was done after 30 min of SRT and as and when required. Chest X-ray 6 h, 24 h after or whenever needed to rule out air leak, pneumonia, and ventilator-associated pneumonia. Bedside cranial ultrasonography was done between 3 and 5 days and at discharge. Those babies who improved gradually without the complication of disease or intervention were weaned from ventilator support and put on oxygen inhalation. Those deteriorated appropriate management was provided with close monitoring of vital signs.

In both groups complications developed, duration of ventilator support, duration of NICU stay, and hospital stay were recorded and summarized. Cost of treatment was not assessed in either group as the study was performed in a government hospital with nominal charges for NICU stay and ventilation.

RESULTS

There were total 103 premature babies; out of the 38 babies meet the SRT criteria and given received the surfactant. The rest of the 65 babies who were also meeting the criteria for SRT but their parents could not afford the surfactant were categorized as nonsurfactant group. General characteristics were the same in both the groups as shown in Table 1. Since it was a tertiary referral center catering babies across the state with poor health transportation, there was a delay in administration of surfactant.

Neonatal deaths were more in the nonsurfactant group (28.95% vs. 50.76%), and the difference was statistically significant (p=0.03). Early neonatal deaths were more in nonsurfactant group (51.51%) than in the surfactant group (36.36%) because of less death from primary issue, i.e., RDS and its complication. Late neonatal deaths were more in the surfactant group (63.63%) than in nonsurfactant group (48.48%); however, the difference was not statistically significant (Table 2).

Table 1: General characteristics of patients

Characteristics	Surfactant (38)	No surfactant (65)
Duration of hospitalization (Mean±SD)	11.15±2.85	11.58±2.93
Gestational age in weeks (Mean±SD)	31.13±1.78	31.16±1.82
Birth weight in grams (Mean±SD)	1227.6±233.12	1293±261.74
Male babies (%)	27 (71.05)	40 (61.53)
Antenatal booked pregnancy (%)	30 (78.94)	47 (72.30)
Antenatal steroid (%) (Last dose 24 h before delivery)	16 (42.10)	25 (38.46)
PROM >18 h (%)	11 (28.94)	18 (27.69)
Cesarean delivery	6 (15.78)	16 (24.61)
Average age at which SRT given	14.15±2.83	

PROM: Premature rupture of membrane, SD: Standard deviation, SRT: Surfactant replacement therapy

Table 2: Early neonatal and late neonatal death

Causes of deaths	Early neonatal deaths			Late neonatal deaths		
	Surfactant group 11 (%)	Nonsurfactant 33 (%)	*p* value	Surfactant group 11 (%)	Nonsurfactant 33 (%)	*p* value
RDS	0	2 (11.76)	1.0	-	-	--
Air leak	1 (25)	2 (11.76)	0.4	0	1 (6.25)	1.0
IVH	0	2 (11.76)	1.0	-	-	--
Sepsis	2 (50)	10 (58.82)	1.0	4 (57.14)	10 (62.50)	1.0
Others (NEC, PPHN, PDA)	1 (25)	1 (5.88)	0.3	0	2 (12.5)	1.0
Pneumonia	-	-	--	3 (42.85)	4 (25)	0.6
Total	4/11 (36.36)	17/33 (51.51)	0.4	7/11 (63.63)	16/33 (48.48)	0.4

RDS: Respiratory distress syndrome, IVH: Intraventricular Hemorrhage, NEC: Necrotizing enterocolitis, PPHN: Persistent pulmonary hypertension of the newborn, PDA: Patent ductus arteriosus

Table 3: Survival rate according to gestational age

Gestational age	Surfactant (38)		Nonsurfactant (65)		*p* value
In weeks	Number	Survival (%)	Number	Survival (%)	
≤27	1	0 (00)	1	0 (00)	--
28–29	7	4 (57.14)	13	4 (30.76)	0.3
30–31	13	9 (69.23)	24	8 (33.33)	0.04
32–33	15	12 (80.00)	17	11 (64.70)	0.4
34	2	2 (100)	10	9 (90.00)	1.0
Total	38	27 (71.05)	65	32 (49.23)	0.03

Table 4: Duration of ventilation, ICU, and hospital stay

Observation	Surfactant group (27)	Nonsurfactant group (32)	*p* value
Duration of ventilation (days)	2.48±0.89	6.09±2.41	0.02
Duration of NICU stay (days)	7.22±2.11	11.96±3.23	0.04
Duration of hospital stay (days)	20.40±6.07	23.65±6.25	0.05

NICU: Neonatal intensive care unit

Table 5: Overall morbidity among survivors

Overall morbidity in survivors	Surfactant group n=27 (%)	Nonsurfactant 32 (%)	*p* value
Sepsis	14 (51.85)	25 (78.12)	0.05
Pneumonia	11 (40.74)	20 (62.50)	0.12
PDA	3 (11.11)	6 (18.75)	0.2
IVH	1 (3.70)	3 (9.37)	0.6
NEC	3 (11.11)	7 (21.87)	0.3
CLD	1 (3.70)	3 (9.33)	0.6
Others (ROP, PPHN, etc.)	3 (11.11)	7 (21.87)	0.3

PDA: Patent ductus arteriosus, IVH: Intraventricular hemorrhage, NEC: Necrotizing enterocolitis, CLD: Chronic lung disease, ROP: Retinopathy of prematurity, PPHN: Persistent pulmonary hypertension of the newborn

Overall, total survival was more in surfactant group (71.05%) than in nonsurfactant group (49.23%) but comparative survival according to gestational age showed the statistically insignificant difference (Table 3). Duration of the ventilation and NICU stay was significantly more in a nonsurfactant group than in babies who received the surfactant (0.02) as shown in Table 4. Overall, morbidities among survivors were more in the nonsurfactant group, but it was non-significant as shown in Table 5.

DISCUSSION

HMD is the most common indication for the neonatal ventilation in our country [9]. The reported survival of babies ventilated for HMD varied from 25% to 64% in our country [10,11]. The survival till discharge in the babies was significantly less in the babies who did not receive surfactant (49.23%), and it was comparable to the other reported studies from India [10,11].

Narang *et al*. [12] in an Indian study found that the early neonatal mortality was significantly lower in surfactant (25%) than in the nonsurfactant group (38.7%) and overall survival till discharge in surfactant group (62.5%) was significantly higher than in nonsurfactant groups (43.7%). Femitha *et al*. [13] in their study found that survival was 71.3% among those who received SRT. Bae *et al*. [15] found neonatal death of 40%. Cummings *et al*. [16] found that the SRT decreased the neonatal mortality up to 40%. This difference was due to the less complication of RDS, less duration of ventilator support and ICU stay, less chances of sepsis, and other complication of supportive therapy in the surfactant group than nonsurfactant group.

Overall, major cause of mortality was sepsis which was more in our study (59%) while it contributed to 49% of neonatal deaths in a study by Narang *et al*. [12]. Bhakoo [17] stated sepsis (67%) was the most common complication of the ventilated babies. In a study by Narang *et al*. [12], early neonatal mortality was significantly lower in a surfactant (25%) than in the nonsurfactant group (38.7%), and septicemia was the most common cause of death in both the groups. The better survival in the surfactant group may be due to the less complication of RDS, duration of ventilation, sepsis, and other intervention.

Sepsis was the most common cause of late neonatal death overall contributing to 59% of the deaths, which was more in comparison to result from other studies. Bae *et al*. [15] in a study in Korea found sepsis as the major cause of mortality (42.6%) in 1996 while Narang *et al*. [12] reported sepsis in 49% of neonatal deaths. The occurrence of infection is directly related to the duration of ventilation and hospital stay, and the lower incidence of sepsis in the surfactant group may be related to the lesser duration of ventilation, ICU stay, less need of intervention, and less complication of the disease process.

In our study, survival was more in steroid plus surfactant (75%) than only steroid (52%). In the study done by Jobe *et al*. [18] concluded that antenatal corticosteroid therapy in threatened premature labor combined with the use of postnatal rescue surfactant is associated with a decreased incidence of RDS and may be beneficial for reducing the severity of RDS and improving the eventual outcome of VLBW infants.

CONCLUSION

Our study showed that a single dose of surfactant given in late hours in established RDS reduced the duration of mechanical ventilation, ICU stay, hospital stay, morbidity, and mortality. Sepsis was the major cause of mortality and morbidity and need to stress on aseptic delivery protocols and neonatal care.

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