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Research Article

Single dose surfactant early rescue therapy in respiratory distress syndrome-experience and outcome at a tertiary care centre

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ABSTRACT

Background: Neonatal respiratory distress syndrome (RDS) is a progressive respiratory failure that is caused primarily by a deficiency of pulmonary surfactants (PS). We undertook a prospective study to evaluate outcomes of neonatal respiratory distress syndrome (RDS) patients treated with early rescue pulmonary surfactant.
Methods: This was a prospective cross sectional study conducted at level III NICU. A total of 47 eligible patients out of 142 diagnosed RDS on chest x-ray or FiO2 ≥40 was needed to reach SpO2 between 85 and 93% received early recue surfactant therapy (within 2hrs of life) and maternal ,neonatal and clinical data was analysed using SPSS software.
Results: In this study prevalence of RDS amongst neonates admitted in NICU was 16.4%, early rescue surfactant therapy could be given only to 47 cases. There was male predominance (2.62:1). Mean age of administration of surfactant was 1.30±0.8 hr and Antenatal steroid was given in only 21.3% of mothers. Fraction of inspired oxygen concentration (Fio_2) requirement also significantly decreases before and after therapy (p value<0.0001) at 6,12, and 24 hrs. PEEP also shows decreasing trend at 24 hrs (p value <0.05). Sepsis was the commonest complication leading to mortality.
Conclusion: Implementation of early rescue administration of surfactant in infants at high risk for developing RDS in neonatal ICU is a safe and effective modality of respiratory support which decreases ventilatory requirements, improves respiratory status, and causes early extubation.

Keywords: Respiratory distress syndrome, Early rescue, Surfactant, Ventilatory parameters, Fraction of inspired oxygen

INTRODUCTION

The neonatal respiratory distress syndrome (RDS) is principally caused by a qualitative and quantitative surfactant deficiency at birth.[1] The first experimental study demonstrating the beneficial effect of surfactant replacement was conducted in the early 1970's by Enhornig G et al by means of the instillation of a natural surfactant, obtained from adult rabbits lungs, into the trachea of preterm rabbits. Subsequently several studies and Meta-analysis have conclusively proven the benefit of this therapy on neonatal mortality and morbidity.[2-7] According to the national neonatal perinatal database 2002-2003, hyaline membrane disease affected 1.2% of total live births and formed 13.5% of total neonatal deaths.[8] A large Proportion of our population is not able to avail surfactant therapy even though it was included in the WHO essential drug list.[9] Two main deterrents to optimal use were non affordability by the patient and non-availability during emergency hours. Different strategies of surfactant instillation include prophylactic approach and early rescue approach. Prophylactic

approach has the advantage of delivering surfactant to alveoli before mechanical ventilation started and better distribution while process of liquid absorption in lung is still occurring.[10]

Early rescue therapy has advantage of instillation of surfactant in stabilized infant and position of endotracheal tube has been verified.[10] The current study was planned to assess and share our experience of early rescue surfactant use in newborn infants with RDS.

METHODS

This was a prospective cross sectional study conducted at level III NICU from July 2003-October 2004. We practiced early rescue surfactant therapy (within 2 hours of life) for those neonates diagnosed with RDS by Chest X ray and who satisfy one of the following: i) Fail to maintain SpO2 above 87%; or Pao2 <50 mm Hg with rising FiO2 requirements on bubble CPAP of 7 cm H2O or ii) recurrent apnea warranting intubation or iii) PaCO2>65 mm Hg or iv) Radiological evidence of Grades III-IV RDS.

Infants with structural cyanotic congenital heart disease, severe congenital malformations, pulmonary hypoplasia, pneumothorax and Apgar scores less than 3 at 5 min were excluded. Exosurf (Burroughs Wellcome Co., USA; dose 5 ml/kg) was administered over a period of 5-10 minutes through a side port adapter.

FiO2 and ventilator settings were immediately adjusted to maintain adequate blood gases (PaO2 50-70 mm Hg, PaCO2 40-50 mm Hg and pH>7.25) with the lowest possible peak inspiratory pressures and FiO2.Routine endotracheal tube suctioning was avoided for the first six hours after surfactant administration.

Blood gases are done 30 minutes post surfactant, and thereafter for change in ventilator parameters or as per clinical requirement. All maternal, perinatal and neonatal data were collected and analyzed using SPSS statistical software. Continuous variables were analyzed using the Student's t or Mann-Whitney test, as appropriate, the significance level was set at $p<0.05$.

RESULTS

There were total 855 admissions in NICU during study period, out of which 16.4% cases (140) developed RDS. Surfactant therapy could be administered in 47(33.6%) cases. Male predominance was seen with a ratio of 2.62:1.

Table 1: characteristics of respiratory distress syndrome neonates.

Characteristics	Number (%)
Total admission in NICU	855
Total cases of RDS	140 (16.4%)
Surfactant recipient	47 (33.6%)
Sex Male Female	 34 13
Mean age of administration of surfactant (hours)	1.30±.8
Antenatal corticosteroid	10 (21.3%)
1' Apgar 5' Apgar	4.8±2.6 7±1.5
Mean gestational age (wks) ≤32weeks ≥32weeks	 30 34.2
Mean birth weight(gms) ≤32weeks ≥32weeks	1256 2036

Table 2: Ventilatory parameters before and after surfactant therapy.

Parameters	Before	After surfactant			P value
		6hr	12hr	24hr	
Frequency(breaths/min)	30±11	30±9.8	29±9.4	25±7.8	0.038
PIP(cm of H_2O)	20±2	21±1.8	21.5±2	20.8±1.9	0.46
PEEP(cm of H_2O)	5±0.3	5.2±0.33	5.8±0.3	5±0.3	0.01
Fio_2	0.83±0.17	0.066±0.2	0.55±0.22	0.43±0.2	0.0001

Table 3: ABG parameters before and after surfactant therapy.

ABG parameters	Before surfactant	After surfactant	P value
PH	7.24±0.18	7.32±0.1	0.986
Pao_2	78±64	108±70	0.32
$Paco_2$	47±18	48±24	0.62
Hco_3^-	9.86±16	22±6	0.2

Mean age of administration of surfactant was 1.30±.8 hr and mean Apgar score at 1 and 5 min was 4.8±2.6 and 7±1.5 respectively. Antenatal steroid was given in only 21.3% of mothers. Mean gestational age (weeks) and birth weight (gms) in ≤32wks cases was 30wk and 1256 gm while in ≥32wks was 34.2 weeks and 2036gm (Table 1).Surfactant was given as single dose rescue therapy in all 47 cases.

Table 4: Outcome of surfactant therapy.

Gestational age	Cases of RDS (n=140)	Surfactant given (n=47)	Survived (n=35)
<28wks	07	04	00
28-30	26	15	11
31-33	43	16	13
≥34	64	12	11

Table 5: characteristics of survivor and non-survivor infants following surfactant therapy.

Characteristics	Survivor(35)	Non –survivor (12)
Mean birth weight	1120±249	1460±210
Mean gestational age	29.8±1.9	30±3.6
Mean Duration of ventilation (hour)	106 ±26.4	120±49.8
Fio_2 at 0 hour 24 hours	 0.83±0.08 0.30±0.18	 0.86±0.13 0.53±0.17
Antenatal steroid	08	02
sepsis	04	07

There was a statistically significant difference in ventilatory rate (breaths/min) before (30±11) and at 24 hr after surfactant therapy (25±7.8, p value<.05). Fraction of inspired oxygen concentration (Fio2) requirement also significantly decreases before and after therapy (p value<0.0001) at 6, 12, and 24 hours PEEP also shows decreasing trend at 24 hours (p value <0.05) but not statistically significant at 6 and 12 hours (Table 2) ABG parameters although showed an improved trend before and after surfactant therapy but was not statistically significant (Table 3).

Overall mortality was 25.5% and was inversely related to gestational age.Fio2 requirement at 24 hr was significantly lower in survivor group. Mean duration of ventilation was 106±26.4and 23% of mother received antenatal steroid in survivor group. Sepsis was the major complication leading to mortality. (Table 4 and 5)

DISCUSSION

The incidence of RDS is reported to be 6.8-14.1% of preterm live births in our country.[8,11] At gestational ages of 29-30 weeks, the incidence is as high as 32% while at ≤28 weeks the incidence is not well documented.[11] RDS is the commonest indication of ventilation in neonates in our country.[12] In our hospital, it was nearly 16.4%. This high incidence can be explained by the very low coverage of antenatal steroids and referral of many high risk mothers. Surfactant trials and clinical experience have demonstrated the synergistic effect of antenatal steroids in reducing incidence, severity of RDS, need for surfactant and mortality.[13]

The coverage of complete course of recommended antenatal steroids among the patients in our study was only 21.3%. All deserving babies could not be given SRT due to practical problems like unaffordability and non-availability of back up ventilator.

Surfactant is one of the expensive modalities for treatment of RDS in premature neonates. But it is proven to be the most effective and standard treatment for RDS in preterm infants in developed countries with significant reduction in mortality and morbidity.[14]

Randomized clinical trials have shown that surfactant therapy in RDS results in an overall 40% reduction in mortality and a 35-50% reduction in air leaks.[15-17] In our study we found that surfactant therapy significantly improves ventilatory parameters before and after surfactant therapy especially significant reduction in Fio2 requirement (p value<0.0001) and ventilatory rate at 24 hours (p value<0.05) thus considerable reduction in baro trauma in these babies.[14]

Surfactant improves oxygenation by increasing lung volume in under aerated regions and by other mechanism.[18-20] Pulmonary under perfusion is one cause of high alveolar ventilation-perfusion ratios (VA/Q)

regions. Accordingly, relief of hypoxemia might reduce high VA/Q regions by countering vasoconstriction, or by allowing mean arterial pressure (MAP) to be reduced (a high MAP would tend to collapse compliant pulmonary vessels). Alternatively, surfactant might normalize high VA/Q regions by reducing regions of the lung which are over ventilated. Rescue surfactant treatment within two hours of life results in decrease in neonatal mortality and bronchopulmonary dysplasia.[21]

Sepsis was the commonest complication in ventilated babies, as high as 67% incidence has been reported.[12] Septicemia has been reported as the commonest cause of mortality in ventilated babies.[22]

Occurrence of infection is directly related to the duration of ventilation and duration of hospital stay. 58.3% of total deaths in this study were directly attributed to septicemia since our patients were from low socioeconomic status and receive poor antenatal care. Although our gestational age specific mortality after surfactant replacement therapy was comparable to previous Indian reports, it was higher than western reports.[23,24]

We face problems of inappropriate nurse: patient ratios and overcrowding. Overall mortality in surfactant recipient neonates was 25.5% which was inversely related to gestational age(25) which is comparable to other studies from developing world (21-80%).(9)The maximum impact on survival was seen in preterm babies(28-33weeks) and very low birth weight (<1500gm).[24]

The successful management of RDS depends on early diagnosis and initiation of treatment. Management of RDS includes invasive and non-invasive mechanical ventilation such as nCPAP.

Surfactant use presupposes the availability of trained personnel to manage neonatal ventilation and facilities to provide total intensive care. Although, surfactant therapy appears very expensive initially, its impact on reducing the duration of ventilation, NICU stay and various morbidities actually decreases the total cost of care.[26,27]

CONCLUSION

Surfactant administration was associated with decreased ventilatory requirements, improved respiratory status, and early extubation. The maximum impact on survival was seen in preterm babies (28-33weeks) and very low birth weight (<1500gm). Sepsis is an important complication and its presence; along with a high RDS score at intubation are significant predictors of mortality.

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