OUTCOME OF SURFACTANT REPLACEMENT THERAPY IN PRETERM BABIES WITH HYALINE MEMBRANE DISEASE AT NEONATAL INTENSIVE CARE UNIT OF A TERTIARY HOSPITAL

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ABSTRACT

Introduction

Hyaline membrane disease (HMD) is an acute lung disease of preterm babies caused by surfactant insufficiency. Decreased surfactant results in insufficient surface tension in the alveolus during expiration leading to alveolar collapse, atelectasis, impaired gas exchange, severe hypoxia and acidosis, leading to respiratory failure. Surfactant replacement therapy (SRT) is now accepted as the standard treatment of preterm babies with HMD.

Objective

The objective of this study was to analyze the outcome of surfactant replacement therapy in preterm babies with hyaline membrane disease.

Methodology

This is a prospective observational study conducted at 10 bedded neonatal unit of Pediatrics Department, Kathmandu Medical College Teaching Hospital, Sinamangal. Study duration was of one year period (15th May 2017 – 14th May 2018). Preterm babies from 26 wks–35 wks of gestation with Hyaline Membrane Disease were included in this study whereas babies with lethal congenital malformations eg: Meningomyelocele, Anencephaly, Gastrochisis, Diaphragmatic Hernia were excluded. All preterm babies who had clinical and radiological features of HMD were considered for Surfactant Replacement Therapy (SRT).

The surfactant (Survanta; Abbott Laboratories, USA; Dose: 4 ml/kg) was administered intra-tracheally according to standard procedures in four divided aliquot applying INSURE (intubation, surfactant administration and extubation to Bubble CPAP) Technique. Ethical clearance was received from Institutional Review Committee (IRC) of Kathmandu Medical College and Statistical analysis was done with SPSS 19 version with frequency and cross tabulation.

Results

In this study of 30 preterm babies with HMD received SRT, 47% (14) were male and 53% (16) were female. The mean birth weight of preterm babies with HMD was 1372.17 ± 395 gms and mean gestational age was 30.1±2.6 weeks. Among 30 preterm babies with HMD receiving SRT, 73.3% (22 babies) discharged from the hospital and 6.3% (8 babies) expired. Among eight expired babies, five died due to pulmonary hemorrhage and three died due to septicemia with DIC. Maximum survival was seen in the gestational age of 30-35 wks and birth weight 1200-2100gms.

Conclusion

The use of SRT has improved the survival outcome and decreased the associated morbidities in babies with HMD. The maximum impact of survival was seen among the preterm babies of 30-35 weeks with birth weight of 1200 -2100 grams.

KEYWORDS

Hyaline Membrane Disease, Preterm babies, Surfactant Replacement Therapy.

INTRODUCTION

In developing countries, neonatal deaths account for more than one third of all deaths in children under the age of five.[1] Mortality rates are very high in the early neonatal period with 25%–45% occurring in the first 24 hours of life, and about 2/3rd of them occurring during the first week of life.[2] Respiratory Distress Syndrome (RDS) or Hyaline Membrane Disease (HMD), has been recognized as the most common complication of prematurity, with more than half of those occurring between birth weight 501-1500 gms showing signs of RDS.[3,4]

Hyaline Membrane Disease (HMD) of the newborn is an acute lung disease of premature babies caused by insufficient surfactant production in alveolus. Insufficient surfactant results in increased surface tension in the alveolus during expiration leading to alveolar collapse, atelectasis, decreased gas exchange, severe hypoxia with acidosis, leading to respiratory failure. In preterm babies with HMD, exogenous surfactant helps to reduce pulmonary air leaks by 50% and neonatal mortality by 30%.[5] Administration of natural surfactant reduces acute respiratory disease, air leaks, bronchopulmonary dysplasia, and mortality in preterm infants.[6] Surfactant replacement therapy (SRT) is now accepted as the standard treatment protocol for preterm babies with HMD.[7] SRT is also helpful for babies with hypoxic respiratory failure, secondary surfactant deficiency in meconium aspiration syndrome, sepsis, pneumonia, and pulmonary hemorrhage.[8] So, the main objective of this study was to analyze the outcome of surfactant replacement therapy in preterm babies with HMD.

METHODOLOGY

This is a prospective observational study done at 10 bedded; level III Neonatal Intensive Care Unit (NICU) of Pediatrics Department, Kathmandu Medical College Teaching Hospital. Perinatal Mortality Rate (PMR) of this tertiary hospital is 10/1000 births and Neonatal mortality rate (NMR) is 4.5 /1000 live births. Total delivery at this hospital is around 4000 per year. The study duration was of one year period (15th May 2017 – 14th May 2018). Preterm babies' with gestational age from 26 –35 wks and birth weight 715-2100 gms with HMD were included in this study whereas preterm babies with lethal congenital anomalies (eg. Meningomyelocel, Anencephaly, Gastrochisis, Diaphragmatic Hernia) were excluded. All preterm babies who had clinical and radiological features of HMD were considered for SRT. For the assessment of respiratory distress in preterm babies, Silverman's Scoring was done at 1 hour of life in all 30 babies.[9]

Under aseptic precautions, the surfactant (Survanta; Abbott Laboratories, USA; Dose: 4 ml/kg) was administered intra-tracheally according to standard procedures in four divided aliquot applying INSURE {intubation, surfactant administration and extubation to Bubble Continuous Positive Airway Pressure (CPAP)} technique.[10] After introduction of surfactant, intermittent inflation breath was given via Ambu Bag. Heart rate, SPO2 and ECG monitoring was done throughout the procedure. Intra tracheally surfactant was given as rescue therapy within 12 hours of birth once specified threshold criteria for diagnosis of HMD was fulfilled. Second dose of Surfactant therapy was considered 12 hours after the first dose, in babies who still need Bubble CPAP (continuous positive airway pressure) or Mechanical Ventilator with Fio_2> 50% and baby is still tachynoic after first dose of SRT. For the diagnosis of HMD in preterm babies following both criteria were used:

1. HMD is an acute lung disease of preterm babies with the classic clinical presentation characterized by a respiratory rate > 60/min, dyspnoea (intercostals, subcostal in drawing, sternal retraction, nasal flaring, cyanosis) with a predominantly diaphragmatic breathing and a characteristic expiratory grunting within 4–6 h of delivery.[11]
2. A chest radiograph consistent with HMD (reticulogranular appearance to lung fields with or without low lung volumes and air bronchograms) within the first 24 hr of life. For practical purposes, the classification of HMD from grade I to III (I – light HMD; II – moderate HMD; III – severe HMD) were done according to the chest x-ray appearance ranging from a light reticulogranular pattern with air bronchograms to whiteout lungs, adapted from the classification of Couchard et al.[12]

Ethical clearance was received from Institutional Review Committee (IRC) of Kathmandu Medical College and written/ verbal informed consent was taken from parents after explaining the benefits and possible complications of surfactant replacement therapy. Statistical analysis was done with SPSS 19 version with frequency and cross tabulation.

RESULTS

In total, 30 preterm babies with HMD who received SRT were included in this study. Among them, 47% (14) were male and 53% (16) were female. Demographics and clinical characteristics of the study population (n= 30) are reported in Table 1. The mean birth weight of preterm babies with HMD receiving SRT was 1372.17 ± 395 gms and mean gestational age was 30.1 ±2.6 weeks. Similarly, mean Silverman's scoring for assessment of respiratory distress at 1 hour of life was 6.07 ± 1.28 and chest retraction, tachypnea with grunting started at 1.83 ±1.14 hr of life. In radiologically 60% (18) of babies were diagnosed as grade III HMD in Chest X-ray. Mean age of 1st dose of SRT for 30 babies were done at 10.17 ± 6.9 hrs of life whereas 8 babies required 2nd dose of SRT at 29.62 ± 12.2 hrs of life. After SRT, the mean duration of preterm babies with HMD kept under Bubble CPAP was 52.40 ± 30.7 hrs whereas mean duration of preterm babies under mechanical ventilation was 6 ± 12.7 hrs.

Table 2 illustrates only 17.7% (5) mothers received two doses of Dexona 12 hrs apart before the delivery of preterm babies. 77.6% (23) preterm babies did not require any form of resuscitation at birth. While analyzing the outcome of SRT among 30 preterm babies, 73.3 %(22) of babies were

discharged whereas 6.3 %(8) babies expired. The mean hospital stay of 22 survived babies was 14.95 ± 6.25days (Table 1). Among survived 22 babies, only 1 baby developed Retina of Prematurity (ROP) whereas five preterm babies died due to Pulmonary Hemorrhage and three babies died due to sepsis with DIC (Disseminated intravascular coagulation) shown in Table 2.

On cross tabulation analysis, Table 3 explains co-relation of birth weight in respect to baby's outcome. Maximum survival was seen among babies with the birth weight of 1200gms and more. Out of 22 survived babies, 15 were with birth weight 1200-2100gms. Similarly, Table 4 explains co-relation of gestational age with respect to baby's outcome. Out of 22 survived babies, 13 preterm babies were of 30-35 wks of gestational age. The result showed maximum survival of babies were found in-between the gestational age 30-35 wks and birth weight 1200-2100gms respectively.

Table 1: Demographics and clinical parameters of babies in NICU (n = 30)

S.N.	Variables	Mean	Range
1	Gestational Age	30.1 ± 2.6 wks	(26 – 35) wks
2	Birth weight	1372.17 ± 395 gms	(715 - 2100)gms
3	Silverman's score at 1 hr of birth	6.07 ± 1.2	(5 -8)
4	Grunting, Tachypnea, chest Retraction started after birth	1.83 ± 1.14 hrs	(1-4) hrs
5	Apgar Score at 1 min	6.03 ± 1.15	(2 – 7)
6.	Apgar Score at 5 min	7.53 ± 0.77	(5-9)
7	Mothers Age	28.03 ± 4.1 yrs	(19 – 39)yrs
8	Duration of Bubble CPAP (with Fio2 Blender)	52.40 ± 30.7 hrs	(10 – 130) hrs
9	Duration of Mechanical Ventilation	6 ± 12.7 hrs	(0- 50)hrs
10	Radiologically Lung expansion duration	34.93 ± 21.4 hrs	(12 -80)hrs
11	1st dose surfactant application (30 babies)	10.17 ± 6.9 hrs	(2 -28) hrs
12	2nd dose surfactant application (8 babies)	29.62 ± 12.2 hrs	(18 -54)hrs
13	Hospital Stay (22 babies)	14.95 ± 6.25 days	(8- 32)days

Table 2: N eonatal parameters (n = 30)

S.N.	Variables	No	(%)
1	**Antenatal 2 doses of Dexona 12 hrs apart**		
	Yes	5	(17.7)
	No	25	(83.3)
	Total	30	(100)
2	**Resuscitation procedure done at birth**		
	Not required	23	(77.6)
	Bag n Mask	6	(20.1)
	Tactile stimulation	1	(3.3)
	Total	30	(100)
3.	**Outcome of preterm babies with HMD**		
	Discharged	22	(73.3)
	Expired	8	(6.3)
	Total	30	(100)
5.	**Morbid condition of survived preterm babies**		
	Normal	21	(95.4)
	Retina of Prematurity (ROP)	1	(4.6)
	Total	22	(100)
6.	**Cause of death**		
	Pulmonary hemorrhage	5	(62.5)
	Sepsis with DIC	3	(37.5)
	Total	8	(100)

Table 3: Cross tabulation on birth weight with respect to outcome of babies (n=30)

	Outcome of babies			
Birth weight (gms)	Discharged	Expired	Total	*p* value
715	1	0	1	0.37
780	0	1	1	
950	0	1	1	
1000	1	2	3	
1020	2	0	2	
1030	1	0	1	
1080	1	0	1	
1100	1	0	1	
1200	4	0	4	
1400	1	0	1	
1420	1	0	1	
1450	1	0	1	
1500	1	0	1	
1520	1	0	1	
1600	1	1	2	
1700	1	0	1	
1780	1	0	1	
1800	1	1	2	
1900	1	0	1	
2000	1	0	1	
2100	0	2	2	
Total	22	8	30	

Table 4: Cross tabulation on Gestational age with respect to outcome of babies : n=30

	Outcome of babies			
Gestational age (wks)	Discharged	Expired	Total	*p* value
26	1	1	2	0.53
27	2	0	2	
28	4	1	5	
29	2	2	4	
30	**6**	**2**	**8**	
31	**0**	**1**	**1**	
32	**2**	**0**	**2**	
33	**1**	**0**	**1**	
34	**1**	**1**	**2**	
35	**3**	**0**	**3**	
Total	**22**	**8**	**30**	

DISCUSSION

HMD is an acute illness in preterm babies due to surfactant insufficiency in lung alveoli. HMD is a major cause of morbidity and mortality in preterm babies. EuroNeoStat Annual Report for Very Low Gestational Age Infants 2010 showed a prevalence of 92% for HMD in newborn babies with a gestational age of 24-25 weeks, 88% at 26-27 weeks, 76% at 28-29 weeks and 57% at 30-31 weeks suggesting HMD incidence is inversely proportional to gestational age i.e less gestational age, more chance of HMD.[13] Surfactant is necessary for inflation of lung alveoli by reducing its surface tension. Clinical trials have confirmed that surfactant replacement therapy is effective in improving the immediate need for respiratory support and the clinical outcome of premature newborns.

Femitha P et al in Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Pondicherry, India, did a study on 101 preterm babies (28 wks – 34 wks) who received SRT as rescue therapy in HMD. The survival rate of preterm babies with SRT was 73.3% (62 babies) and found sepsis (43.5%), apnea (4.9%) and pulmonary hemorrhage (3.9%) as a co-morbid condition. It was very apathetic that only 20.8% mother received complete course of antenatal steroids.[14] Similarly, in this study (at Kathmandu Medical College Teaching Hospital), survival rate after SRT in preterm babies with HMD was 73.3% (22 out of 30 preterm babies) and common co-morbid condition observed were pulmonary hemorrhage (62.5%) and Sepsis with DIC (37.5%). It was also so apathetic that only 17.7% (5) mothers received complete course (2 doses 24 hours apart) of Dexona before the delivery of their baby.

In another study by Narang A et al in Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India, received 88 preterm babies with surfactant replacement therapy. The mean gestational age was 30.7±2 wks and mean birth weight was 1387±46 gms with survival rate was 75% and mean hospital stay was 14.5±12.1 days.[15] In this study at Kathmandu Medical College Teaching Hospital, mean birth weight of babies receiving SRT was 1372.17 ± 395 gms, mean gestational age 30.1 ±2.6 weeks and mean hospital stay 14.95 ± 6.25 days suggestive of comparable outcomes in both studies. Survival outcome in this study showed birth weight≥ 1200 gms and gestation ≥ 30wks, which was quite similar to the Narang A et al study (Gestational age ≥ 30 wks and birth weight≥ 1000gms).

A multi centre study in Newyork by Kendig JW et al has shown "rescue" surfactant replacement therapy is equally efficacious and comparable as early 'prophylactic' surfactant replacement therapy for preterm babies with HMD.[16] So, in developing countries like Nepal, due to lack of affordability, "rescue" surfactant replacement therapy is usually practiced and in this study at Kathmandu Medical College Teaching Hospital also "rescue" surfactant replacement therapy among 30 preterm babies with HMD was practiced..

CONCLUSION

Probably this is the first study done in Nepal highlighting the positive impact of SRT in preterm babies with HMD. The use of SRT has improved the survival outcome and decreased the associated morbidities in babies with HMD. The maximum impact of survival was seen among the preterm babies of 30-35 weeks gestation and birth weight group of 1200 -2100 grams. This study has also shown that SRT followed by Bubble CPAP has significantly reduced the subsequent need for mechanical ventilation.

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CONFLICT OF INTEREST

I declare no conflict of Interest

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