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Effect of Early and Prophylactic Surfactant Therapy in Preterm Neonates in a Tertiary Care Setting: A Clinical Study

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Abstract

Context: Respiratory Distress Syndrome (RDS) is a significant cause of morbidity and mortality in preterm neonates due to pulmonary immaturity and lack of endogenous surfactant. This study evaluates the effect of early and prophylactic surfactant therapy in preterm neonates in a tertiary care setting.

Aims: To assess the clinical outcomes of early and prophylactic surfactant therapy in preterm neonates.

Settings and Design: A prospective observational clinical trial conducted over 24 months at the Neonatal Intensive Care Unit (NICU) of VMGMC Solapur.

Methods and Material: The study included preterm neonates up to 28 days old who received surfactant therapy. Neonates with severe congenital anomalies were excluded. Surfactant was administered using the Intubation-surfactant-Extubation (InSurE) technique without sedation. Bovine lipid extract surfactant (NEOSURF) was administered, followed by non-invasive positive pressure ventilation (NIPPV). Data was collected using a pre-designed questionnaire and analysed using IBM SPSS version 21.0.

Statistical analysis used: Descriptive statistics was used to describe the data. Chisquare test was applied for qualitative data, and Student's t-test for quantitative data. A pvalue of <0.05 was considered statistically significant.

Results: Out of 97 neonates, 67.01% had a gestational age of 28-32 weeks, and 62.88% had low birth weight. Clinical presentations included nasal flaring (97.93%) and grunting (63.91%). The majority of surfactant administrations occurred within the first 6 hours (53.6%). Postsurfactant, arterial blood gas normalization was achieved in 88% of the cases. Complications included acute desaturation (12.37%) and apnea (12.37%). Mortality was 10.67%, with the majority being discharged after an average NICU stay of 17.6 days.

Conclusions: Early and prophylactic surfactant therapy significantly improved clinical outcomes in preterm neonates, reducing morbidity and mortality with manageable complications.

Keywords: Preterm neonates, Respiratory Distress Syndrome, Surfactant therapy, Insure technique, NICU.

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Key Messages: Early surfactant therapy is effective in improving outcomes in preterm neonates, with reduced morbidity and manageable complications, underscoring its importance in neonatal care.

INTRODUCTION

Respiratory distress syndrome (RDS) is a disease observed in neonates with pulmonary immaturity. It is caused due to the lack of an endogenous surfactant, normally produced by the lungs.[1] Surfactant is responsible for facilitating and maintaining inflation of the lower airways and diffusion of oxygen into the pulmonary capillaries. Without it, breathing is nearly impossible and symptoms such as accessory muscle use, cyanosis, and tachypnoea ensue rapidly after birth.[2] Former treatment methods consisted mostly mechanical ventilation and oxygen therapy; today however, treatment involves the administration of an exogenous form of surfactant.[3] The development of exogenous surfactant therapy has decreased the morbidity and mortality rates of neonates with RDS immensely; because of its institution in most neonatal care environments, RDS is rarely manifested in otherwise healthy neonates beyond their first few hours of life.[4,5]

Exogenous surfactant preparations must spread rapidly and efficiently into the air-liquid interface once instilled in the proximal airways, with the goal of achieving a homogenous distribution throughout the lungs.[6] However, rapid administration of liquid into the lungs may elicit transient oxygen desaturation and bradycardia, or significant complications such as severe airway obstruction, pulmonary haemorrhage, pneumothorax or pulmonary hypertension.[7] Therefore, surfactant should be administered according to a wellestablished protocol under the supervision of clinicians and respiratory therapists experienced in tracheal intubation, ventilator management and general care of the premature infant.[8]

MATERIALS AND METHODS

Prospective observational clinical trial was conducted over a period of 24 months from October 2019 to September 2021 at VMGMC Solapur (MS), after institutional ethics committee approval. All study participants were admitted in the NICU. All preterm neonates up to 28 days age was the study population. All preterm neonates who received surfactant therapy were included in the study. Consent from either of the parents was taken before enrolling into the study, preterm with Silverman Anderson score >7.

CXR suggestive of RDS, desaturation was included into the study. Neonates with severe congenital anomalies were excluded from the study. The information regarding the study variables was recorded on a predesigned, pretested questionnaire. Physical examination was done after the interview. The investigations such as haemoglobin, blood group, urine sugar and albumin, etc. were done.

In Intubation alongside the application of Surfactant and then Extubation (Insure technique), infants were intubated with an appropriate size endotracheal tube. No sedation or premedication was used but nesting and swaddling was done during the procedure. For surfactant replacement therapy, Bovine Lipid extract (NEOSURF) (BLES Biochemicals Inc. London, Canada N5V3KA, Imported and marketed by cipla) (135 mg/ kg), was administered with positive pressure ventilation with an appropriate size self-inflating resuscitation bag. Babies were extubated immediately after few minutes of surfactant administration and after extubation, infants were put on Non-invasive positive pressure ventilation (NIPPV) again. The criteria for subsequent doses of surfactant, requirement of intubation as failure and weaning were same as mentioned in standard guidelines.

All data was collected and complied in Microsoft excel. All statistical analyses were performed by using IBM SPSS statistics Version 21.0 (SPSS Inc., Chicago, IL, USA) and open epi version 2.3.1. Descriptive statistics such as percentage (%), mean, range and standard deviation (SD) were used to describe the data. Chi square test was applied for qualitative data and student t test for quantitative type of data. A p value of <0.05 was regarded as statistically significant.

RESULTS

Table 1 shows total 97 neonates were studied. The majority of neonates had gestational age between 28 to 32 weeks (67.01%) and were predominantly male (67.01%). Birth weight distribution included 11.34% with extremely low birth weight, 22.68% with very low birth weight, 62.88% with low birth weight, and 3.09% with normal birth weight. Vaginal delivery occurred in 60.82% of cases. Antenatal use of steroids was observed in 54.63% of neonates.

Table 1: Baseline characteristic of study participants

Variables	Frequency (n=97)	Percentage
Gestational age in weeks		
28 to 32	65	67.01
32 to 34	20	20.61
>34	12	12.37
28 to 32	65	67.01
Gender		
Male	65	67.01
Female	32	32.99
Birth weight in kg		
Extremely low birth weight (<1)	11	11.34
Very low birth weight (1 to 1.5)	22	22.68
Low birth weight (1.5 to 2.5)	61	62.88
Normal birth weight (>2.5)	3	3.09
Mode of delivery		
Vaginal	59	60.82
LSCS	38	39.18
Antenatal use of steroids		
Yes	53	54.63
No	44	45.36

Table 2: Clinical Characteristics and Surfactant Administration

Variables	Frequency(%)
APGAR Score (mean ± SD)	
At 1 min	1.3 ± 6.1
At 5 min	1.0 7.6±
Clinical presentation	
Nasal flaring	(97.33%) 95
Grunting	(63.91%) 62
Chest retraction	(55.67%) 54
Cyanosis	(25.77%) 25
Silverman anderson score	
to 5-6	(12.3%) 12
to 7-8	(63.9%) 62
to 9-10	(23.7%) 23
Age in hours at time of surfactant administration	
0-6	(53.6%) 52
to 6 - 24	(36.1%) 35
to 24 - 48	(10.3%) 10
Doses of surfactant given with Insure tech with CPAP (n:97)	
Single Dose	(88.6%) 86
Two dose	(11.4%) 11
Doses of surfactant given in patient with Ventilator support for >6 hours (n:13)	
Single Dose	(69.2%) 9
Two Dose	4 (30.8%)

The mean APGAR scores at 1 minute and 5 minutes were 6.1 and 7.6, respectively. Predominant clinical presentations included nasal flaring (97.93%), grunting (63.91%), chest retraction (55.67%), and cyanosis (25.77%). Silverman Anderson scores distributed as 12.3% (5 to 6), 63.9% (7 to 8), and 23.7% (9 to 10). The majority of surfactant administrations occurred within the first 6 hours (53.6%). (from table 2)

Table 3: Oxygen Support, ABG Normalization, and Complications

Outcomes after Surfactant Therapy			
Outcome	**O2 hood (n:17)**	**CPAP (n:58)**	**Ventilator (n:22)**
Improved	4	18	2
O2 hood	3	20	5
Cpap	6	10	5
Ventilator	4	9	7
Death	0	1	3
Normalization of ABG after giving surfactant in preterm			
ABG	**PaO2**	**PCO2**	**P/F ratio**
Normal	86	88	95
Abnormal	11	9	2
Complications associated with surfactant therapy in preterm,			
Complication	**Frequency**		
Acute desaturation	12 (12.37%)		
Apnea	12 (12.37%)		
Acute bradycardia	10 (10.3%)		
Pulmonary haemorrhage	6 (6.18%)		
Air leak	4 (4.12%)		
Pneumothorax	3 (3.09%)		

Table 3 shows post-surfactant, improvements were observed in 24 cases, with varying support modalities (O2 hood, CPAP, ventilator, and unfortunately, 4 cases resulted in death). Statistical significance was seen, p=0.02. between pre-surfactant and Post surfactant O2 support. Short term outcome (48hrs) with respect to oxygen and respiratory support post surfactant therapy in preterm ABG normalization was achieved in 88% of cases, with normal PaO2 (86%), PCO2 (88%), and P/F ratio (>95). Complications associated with surfactant therapy included acute desaturation (12.37%), apnoea (12.37%), acute bradycardia (10.3%), pulmonary haemorrhage (6.18%), air leak (4.12%), and pneumothorax (3.09%).

DISCUSSION

In the present study, the focus was on neonates receiving surfactant therapy, with a significant majority (64.67%) being preterm. The majority of preterm infants (67.01%) in our study had a gestational age between 28 to 32 weeks. This finding aligns with other studies, such as Farhan A *et al*.[9] which reported a mean gestational age of 30 weeks in their study, and Gp Capt Daljit Singh *et al*.[10] who found a mean gestational age of 28.64 weeks among preterm infants. Among preterm infants, 67.01% were males, and 32.99% were females. These results differ slightly from other studies, with variations in gender distribution reported by different studies.[9–11] The majority of preterm infants (62.88%) in our study had low birth weight. These findings are consistent with previous studies, with Gp Capt Daljit Singh *et al*.[10] reporting a mean birth weight of 1030 grams among preterm infants. Vaginal delivery was more prevalent among preterm infants in our study (60.82%). This aligns with findings from a study by David *et al*.[12] which showed a majority of vaginal deliveries compared to C-section. Mean APGAR scores at 1 and 5 minutes were within acceptable ranges for preterm infants in our study. The comparison with Farhan A *et al*.[9] demonstrated variations in APGAR scores at 1 and 6 minutes. Nasal flaring, grunting, chest retraction, and cyanosis were common clinical presentations among preterm infants. These findings are in line with studies by other authors. Silverman-Anderson score for preterm infants indicated varying degrees of respiratory distress. Approximately 54.63% of preterm infants in our study had antenatal steroid use, consistent with findings by David *et al*.[12] who reported 79.9% antenatal steroid use. In preterm infants, surfactant administration within the first 24 hours of life was common. These findings are vital for assessing the efficacy of surfactant therapy. Different dosages were administered based on the clinical condition, with Insure technique and CPAP being significant among preterm infants. Short-term outcomes within 48 hours post-surfactant therapy showed varying degrees of improvement in preterm infants. After surfactant therapy, improvements were observed in arterial blood gas parameters for preterm infants, consistent with findings from Farhan A *et al*.[9] Complications such as acute desaturation, apnea, bradycardia, pulmonary hemorrhage, air leak, and pneumothorax were noted. These findings are consistent with studies by Gp Capt Daljit Singh *et al*.[10] and CK Natarajan *et al*.[13] The mean duration of NICU stay was longer for preterm infants (17.6 days), aligning with previous studies reporting variable lengths of hospital stays. Multifactorial causes contributed to mortality, with septic shock being the most common cause among preterm infants. No statistical significance was observed in the duration of ventilator support among preterm infants. Overall, 10.67% mortality was observed among preterm infants, with the majority being discharged. This aligns with findings from other studies indicating varying mortality rates.[14]

CONCLUSION

In conclusion, our study contributes valuable insights into the demographic profile, clinical characteristics, and outcomes of preterm infants receiving surfactant therapy. In Preterm neonates, early and prophylactic surfactant therapy was effective and improved outcome with less morbidity and mortality and less complications. Further, research and collaborative efforts are essential for refining treatment strategies and improving the overall care of these vulnerable neonates.

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Conflict of Interest: Nil

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