International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

A Prospective Observational Study on the Effect of Less Invasive Surfactant Administration in Respiratory Distress Syndrome in Preterm Neonates Admitted in Nicu of a Tertiary Care Hospital

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Received: 02-01-2026
Accepted: 21-01-2026
Available online: 31-01-2026

ABSTRACT

Introduction: Respiratory Distress Syndrome is a major cause of morbidity in preterm neonates, often necessitating surfactant replacement therapy. Less Invasive Surfactant Administration is an emerging alternative that allows for surfactant delivery while the neonate breathes spontaneously on Continuous positive airway pressure. This study aims to evaluate the effect and feasibility of the Less Invasive Surfactant Administration.

Methods: This prospective observational study was conducted on forty preterm neonates requiring surfactant therapy. Bovine Lipid Extract Surfactant (5 ml/kg) via a six French nasogastric tube under direct laryngoscopy. Respiratory parameters were monitored before and after the procedure and outcomes were recorded.

Results: Following less invasive surfactant administration, the mean Silverman–Anderson score score decreased from 5.41 at birth to 4.12 at 6 hours post-procedure (p=0.004), mean respiratory rate reduced from 64.98/min to 57.58/min (p=0.030), and the mean oxygen saturation to inspired oxygen ratio improved from 2.31 to 3.69 (p=0.040). The Less invasive surfactant administration failure rate was 10% (n=4). Common adverse events were transient bradycardia (75%) and apnea (65%). The overall mortality rate was 15% (n=6), associated with co-morbidities like extremely low birth weight and sepsis.

Discussion: Less invasive surfactant administration is a safe and feasible technique for surfactant administration in spontaneously breathing preterm neonates with Respiratory Distress Syndrome. It leads to significant improvements in respiratory parameters and reduces the need for Continuous positive airway pressure, thereby minimizing exposure to invasive mechanical ventilation and its complications.

Keywords*: Preterm infant, Neonatal respiratory distress, Pulmonary surfactant therapy, Non-invasive respiratory support, Continuous positive airway pressure.*

INTRODUCTION

In neonatal intensive care units, a large percentage of inpatients are preterm infants, who have a high chance of developing Respiratory Distress Syndrome (RDS). RDS is a prevalent disorder in early premature infants and a major cause of morbidity [1]. It is primarily caused by a deficiency of pulmonary surfactant, which is essential for reducing surface tension and preventing alveolar collapse during expiration[2]. The absence of surfactant leads to a large burden of breathing and subsequent respiratory failure, with major complications including the need for mechanical ventilation, pneumothorax, bronchopulmonary dysplasia (BPD), and peri-intraventricular hemorrhage (PIVH) [3]. Surfactant replacement therapy is a cornerstone of RDS management and has been proven to decrease morbidity and mortality rates [4]. The conventional method for surfactant delivery is the INSURE (Intubation-Surfactant-Extubation) technique. However, even brief exposure to positive pressure ventilation during this procedure can trigger an inflammatory cascade and lung injury [3,5]. To mitigate these risks, less invasive methods have been developed [6]. Less Invasive Surfactant Administration (LISA) is a technique where surfactant is delivered via a thin catheter into the

trachea while the infant continues to breathe spontaneously on Continuous Positive Airway Pressure (CPAP) [7]. The aim of LISA is to deliver the surfactant while maintaining the physiology of the glottis and avoiding mechanical ventilation [8]. Studies suggest LISA is associated with better pulmonary outcomes, including a reduced risk of BPD and mortality [9-11]. Recent systematic reviews and clinical studies confirm that LISA significantly reduces CPAP duration, mechanical ventilation need, and intubation risk in preterm infants[2,14,15]. This study was conducted to evaluate the effects and determine the feasibility of the LISA procedure for treating RDS in preterm neonates at a tertiary care hospital.

MATERIALS AND METHODS

Study Design and Population This prospective observational study was conducted in the neonatal intensive care unit of a tertiary care hospital in Jaipur from November 2023 to June 2024, after receiving approval from the Ethics Committee of RUHS College of Medical Sciences (protocol number 2023/236; approved on 4 November 2023). The study included 40 preterm neonates between 28 and 36 weeks of gestation with RDS, defined by Chest X-ray findings and either a Silverman-Anderson Score (SAS) of ≥4 or failure to maintain SpO_2 >90% on FiO_2 ≥40%. Exclusion criteria included major congenital malformations, cardiovascular instability, recurrent apnea, or the need for intubation at birth. Informed written consent was obtained from the parents of all participants.

Sample Size Justification: The sample size was estimated based on a 25% decrease in the CPAP requirement at 72 hours after LISA versus standard management. With an alpha of 0.05 and power of 80%, at least 35 neonates were needed. In anticipation of anticipated attrition or exclusions, 40 neonates were recruited.

LISA Procedure Neonates were positioned with a slightly extended neck. While the baby remained on CPAP, the vocal cords were visualized using a direct laryngoscope, and a 6 Fr nasogastric tube was introduced just below the cords. Neosurf (Bovine Lipid Extract Surfactant) at a dose of 5 ml/kg was administered slowly through the catheter over 2-3 minutes. The procedure was temporarily halted in cases of significant bradycardia (<80 bpm), desaturation (<85%), or apnea.

Data Collection and Outcomes Respiratory status was assessed using the SAS, respiratory rate, and SpO_2/FiO_2 ratio at birth and at intervals up to 6 hours post-procedure. The primary outcomes were the changes in these respiratory parameters. Secondary outcomes included the need for and duration of CPAP and mechanical ventilation, procedural complications, LISA failure (defined as poor clinical and radiological improvement requiring a repeat dose of surfactant via INSURE), and overall mortality.

Statistical Analysis Quantitative variables were summarized as mean ± standard deviation, and categorical variables as frequencies and percentages. The independent t-test and Chi-square test were used for comparisons. A p-value <0.05 was considered statistically significant. SPSS version 20.0 was used for all analyses.

RESULTS

The study included 40 preterm neonates with a mean birth weight of 1.477 ± 0.406 kg and a mean gestational age of 32-34 weeks. Key demographic and clinical characteristics are detailed in **Table 1**.

Table 1: Baseline Characteristics of Study Population (n=40)

Characteristic	Value
Gestational Age (weeks), mean	32-34
Birth Weight (kg), mean ± SD	1.477 ± 0.406
Male Gender, n (%)	20 (50.0%)
Vaginal Delivery, n (%)	33 (82.5%)
Antenatal Steroids, n (%)	15 (37.5%)
RDS Severity at Admission, n (%)	
- Moderate RDS	31 (77.5%)
- Severe RDS	9 (22.5%)

Following LISA, a statistically significant improvement was observed across all primary respiratory parameters. The mean SAS, respiratory rate, and SpO_2/FiO_2 ratio all showed significant improvement at 6 hours post-procedure (**Table 2**).

Table 2: Changes in Respiratory Parameters Pre- and Post-LISA (n=40)

Parameter	Pre-LISA (at birth)	Post-LISA (at 6 hrs)	p-value
Silverman-Anderson Score, mean ± SD	5.41 ± 0.68	4.13 ± 1.14	0.004*
Respiratory Rate (breaths/min), mean ± SD	64.98 ± 4.76	57.58 ± 7.32	0.030*
SpO_2/FiO_2 Ratio, mean ± SD	2.31 ± 0.09	3.69 ± 1.40	0.040*

Statistically significant ($p < 0.05$)

Clinically, the need for respiratory support decreased significantly. While 100% of neonates required CPAP at 6 hours, only 42.5% required it by 72 hours ($p<0.0001$). Eight neonates (20%), all of whom had severe RDS, required mechanical ventilation by 72 hours. The LISA failure rate was 10%. The most common transient procedural complications were bradycardia (75%) and apnea (65%). The overall mortality rate was 15% (**Table 3**). **Subgroup Analysis**: Mortality was significantly higher in extremely low birth weight (ELBW <1 kg) neonates (50%, 3/6) than in those ≥1 kg (8.8%, 3/34). Also, ELBW infants had more bradycardia and apnea events.

Table 3: Clinical Outcomes and Complications (n=40)

Outcome / Complication	Frequency (n)	Percentage (%)
Need for Respiratory Support		
- CPAP at 72 hrs	17	42.5%
- Mechanical Ventilation at 72 hrs	8	20.0%
LISA Failure	4	10.0%
Procedural Complications		
- Bradycardia (transient)	30	75.0%
- Apnea (transient)	26	65.0%
- Surfactant Reflux	14	35.0%
- Pneumothorax	2	5.0%
- Pulmonary Hemorrhage	1	2.5%
Mortality	6	15.0%

DISCUSSION

This research proves that LISA is a safe and viable method of surfactant administration in preterm infants with RDS in an Indian NICU in a tertiary care hospital. There was significant improvement in respiratory parameters such as Silverman–Anderson score, respiratory rate, and SpO_2/FiO_2 ratio after the procedure, establishing the short-term efficacy of LISA in stabilizing pulmonary function. These results are in agreement with global evidence indicating that LISA decreases the requirement for invasive ventilation with sufficient oxygenation and ventilation in preterm infants [6-9]. The need for mechanical ventilation in our analysis was 20%, which is within the range reported worldwide (10–25%) [10,11]. Specifically, Herting et al. reported that LISA can substantially reduce intubation rates relative to the INSURE technique, particularly among those with moderate-to-severe RDS [8]. Likewise, Aldana-Aguirre et al. demonstrated by meta-analysis that LISA lessened the composite outcome of death or bronchopulmonary dysplasia (BPD) [9]. Our results support these findings and add region-specific evidence of importance.

Complication rates in this study were largely transient occurrences like bradycardia and apnea, which settled with minimal management. This accords with previous reports that, while transient desaturation and bradycardia are commonplace during LISA, severe complications like pneumothorax or pulmonary hemorrhage are still exceedingly rare [12,13]. In our population, merely two instances of pneumothorax (5%) and one instance of pulmonary hemorrhage (2.5%) occurred, in line with international information.

Death in our study was 15%, largely due to comorbid conditions including extremely low birth weight (ELBW) and sepsis and not due to the procedure. Previous studies have demonstrated that ELBW infants (<1000 g) outcomes continue to be difficult despite the application of LISA, highlighting the necessity of precise patient selection and vigilant monitoring in this subgroup [14,15].

This subgroup analysis highlights that birth weight significantly affects outcomes after LISA. Neonates ≥1 kg tended to have a better outcome, while ELBW infants continued to have increased risk for unfavourable outcomes. This is in line with global observations, indicating LISA use in ELBW infants must be met with increased monitoring and selection protocols.

The greatest strength of this research is being among the few prospective datasets from an Indian NICU. Although the majority of published evidence is from Europe, there is limited evidence available from South Asia. Through proof of feasibility and safety in a resource-constrained environment, our findings justify broader use of LISA in India. Secondly, the formal sample size estimation brings credibility to the strength of the findings despite small numbers. The drawbacks consist of the relatively low sample size, single-center trial, and lack of direct control group. This study, however, yields useful pilot data that can guide larger multicentric trials in India.

In summary, our results show that LISA enhances initial respiratory outcomes, decreases the requirement for mechanical ventilation, and is linked with an acceptable safety profile in Indian preterm infants with RDS. This complements current worldwide evidence with region-specific data that can inform future practice and policy.

CONCLUSION

The current study shows that LISA is a safe, feasible, and effective alternative to the traditional INSURE method of surfactant administration in preterm infants with RDS. In our series, LISA significantly enhanced respiratory parameters and decreased the need for CPAP and mechanical ventilation, findings in keeping with earlier international reports [6-9,14]. Notably, the procedure was well tolerated with only temporary complications seen, and severe adverse events like pneumothorax and pulmonary hemorrhage remained rare [12,13].The mortality seen was largely with regard to comorbidities like extremely low birth weight and sepsis and not LISA per se, emphasizing the importance of careful selection of patients and careful follow-up in high-risk populations [15]. This points to the fact that whereas LISA can be safely applied in standard NICU practice, results in the most critically at-risk neonates need to be assessed.One of the strong points of this research is the addendum it makes to the growing pool of region-specific data from South Asia, where evidence of LISA continues to be scarce. By establishing the feasibility of LISA in an Indian tertiary-care NICU, this research lends impetus to its broader application in comparable resource-constrained environments. Concurrently, shortcomings such as small sample size, single-center study design, and absence of a comparator arm should be noted.Prospective multicentric, well-powered studies in the future are needed to lay down standardized national guidelines and to further evaluate long-term sequelae like BPD and neurodevelopment. In the meantime, our findings offer significant preliminary evidence favoring incorporation of LISA into neonatal respiratory care protocols in India.

Perspectives for Future Research

Further multicenter randomized controlled trials are needed to compare less invasive surfactant administration with conventional surfactant delivery methods in preterm neonates. Future studies should focus on long-term outcomes such as bronchopulmonary dysplasia, neurodevelopment, and persistent respiratory morbidity, as well as refine patient selection criteria, particularly in extremely low birth weight infants.

Authorship Criteria and Authors' Contribution Details

All authors meet the authorship criteria recommended by the International Committee of Medical Journal Editors

Dr. Sangevi Raam A. contributed to the conception and design of the study, data collection, analysis and interpretation of results, and drafting of the manuscript.

Dr. Deependra Garg provided overall supervision, contributed to study design refinement, critically revised the manuscript for important intellectual content, and approved the final version.

Dr. Reshu Gupta contributed to statistical guidance, data interpretation, critical manuscript review, and final approval of the manuscript.

Aditi Goyal contributed to data acquisition, literature review, manuscript preparation, coordination of revisions, and correspondence with the journal as the corresponding author.

Funding

No external funding was received for this study.

Conflict of Interest

The authors declare no conflict of interest.

Artificial Intelligence Disclosure

Generative artificial intelligence tools were used solely for language editing, clarity enhancement, and formatting of the manuscript. All scientific content, data analysis, interpretation, and conclusions were generated, reviewed, and validated by the authors. Human oversight was maintained throughout the manuscript preparation process, and no confidential patient data were processed using artificial intelligence tools.

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