

# Techniques Of Surfactant Administration And Their Effect On Outcomes In Preterm Neonates With Respiratory Distress Syndrome

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## Abstract:

**Background:** Respiratory Distress Syndrome (RDS) in premature infants results from surfactant deficiency and remains a major cause of early neonatal morbidity and mortality. Surfactant replacement therapy has significantly improved outcomes, and newer methods aim to reduce invasiveness and procedure-related complications. This study compares the outcomes of two surfactant administration techniques: INTubation–SURfactant–Extubation (INSURE) and Less Invasive Surfactant Administration (LISA).

**Materials and Methods:** A retrospective observational study was conducted on 90 preterm neonates (28–34 weeks gestation) diagnosed with RDS and admitted between January and June 2021. Infants with congenital lung malformations or congenital heart disease were excluded. Surfactant (Survanta, 100 mg/kg) was administered via LISA (n = 50) or INSURE (n = 40). Outcomes assessed included reintubation within 72 hours and mortality. Statistical analysis was performed using the Chi-square test, with  $p < 0.05$  considered significant.

**Results:** Gestational age ( $p = 0.10$ ) and birth weight ( $p = 0.082$ ) did not influence the method of surfactant administration. Reintubation rates were similar between groups—50% in the INSURE group and 46% in the LISA group ( $p = 0.705$ ). Mortality was significantly higher in the INSURE group, with LISA demonstrating superior survival outcomes ( $p = 0.00044$ ).

**Conclusion:** LISA is associated with significantly lower mortality compared with INSURE, without differences in reintubation rates. LISA appears to be a superior modality for surfactant administration in preterm neonates with RDS.

**Key Word:** INSURE; LISA; Respiratory Distress Syndrome; Surfactant; Preterm Neonates

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## I. Introduction

Respiratory Distress Syndrome (RDS) remains one of the most common causes of early morbidity and mortality in preterm neonates. It primarily results from pulmonary immaturity and deficiency of endogenous surfactant, leading to alveolar collapse, impaired gas exchange, and progressive respiratory failure [1]. The incidence and severity of RDS are inversely related to gestational age, making it a significant challenge in the care of premature infants, particularly those born before 34 weeks of gestation [2].

The introduction of exogenous surfactant therapy in the early 1990s represented a major breakthrough in neonatal medicine and has since led to a substantial reduction in mortality and complications associated with RDS [3]. Traditionally, surfactant has been administered via endotracheal intubation followed by mechanical ventilation, commonly referred to as the INTubation–SURfactant–Extubation (INSURE) technique. While effective, this approach exposes fragile preterm lungs to positive pressure ventilation, increasing the risk of barotrauma, volutrauma, and the subsequent development of bronchopulmonary dysplasia [4].

In an effort to minimize ventilator-induced lung injury, strategies promoting non-invasive respiratory support have gained prominence. The SUPPORT trial demonstrated that early use of continuous positive airway pressure (CPAP) could reduce the need for mechanical ventilation without adversely affecting survival [5]. Building on this concept, Less Invasive Surfactant Administration (LISA) was developed, wherein surfactant is delivered through a thin catheter while the infant continues spontaneous breathing on CPAP [6]. This technique aims to combine the benefits of surfactant therapy with lung-protective ventilation strategies.

Although multiple studies from high-income settings suggest improved outcomes with LISA, data from resource-limited settings remain limited [7]. Real-world comparisons of INSURE and LISA are therefore

essential to guide evidence-based decision-making. The present study was undertaken to compare these two techniques in preterm neonates with RDS, focusing on mortality and reintubation rates.

## **II. Material And Methods**

### **Study Design and Setting**

This retrospective observational study was conducted in the neonatal intensive care unit (NICU) of a tertiary care center.

### **Study Population**

A total of 90 preterm neonates born between 28–34 weeks gestation and diagnosed with RDS from January to June 2021 were included.

### **Inclusion Criteria**

- Preterm infants (28–34 weeks gestation)
- Clinical and radiological diagnosis of RDS
- Received exogenous surfactant

### **Exclusion Criteria**

- Congenital lung malformations
- Congenital heart disease

### **Intervention**

All infants received Surfactant (beractant) at a dose of 100 mg/kg via one of two techniques:

LISA group: n = 50

INSURE group: n = 40

### **Outcome Measures**

#### **Primary outcomes:**

- Requirement of reintubation within 72 hours
- Mortality

#### **Secondary variables:**

- Influence of gestational age
- Influence of birth weight

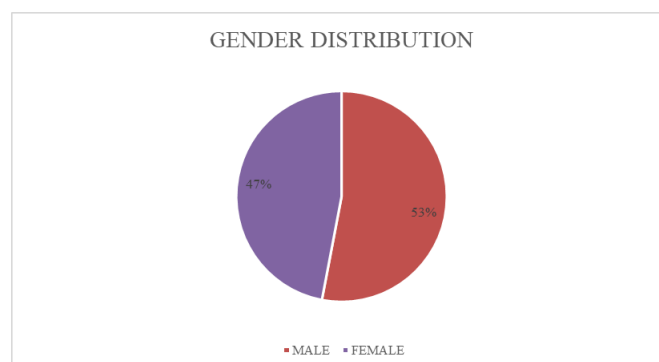
### **Statistical Analysis**

Categorical variables were analyzed using the Chi-square test. Degrees of freedom and critical values were calculated to determine significance. A p-value < 0.05 was considered statistically significant. Data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL).

## **III. Results**

### **Demographic Characteristics**

- Male: 53% (n = 48)
- Female: 47% (n = 42)



**Figure no 1,** Shows the gender distribution pattern of the newborns included in the study, i.e. it included 53% male preterm neonates and 47% female preterm neonates.

**Table no 1. Influence of Gestational Age on Method of Surfactant Administration**

Gestational age->	Less than 28 weeks	28-32 weeks	32-37 weeks	Total
INSURE [n, (%)]	13(32.5%)	19(47.5%)	8(20%)	40(44.4%)
LISA [n, (%)]	7(14%)	28(56%)	15(30%)	50(55.6%)
Total [n, (%)]	20(22.2%)	47(52.2%)	23(25.6%)	90(100%)

**Table no 1**, illustrates the distribution of preterm neonates across different gestational age categories according to the method of surfactant administration (INSURE versus LISA).

Although a higher proportion of infants in the 28-32 weeks and 32-37 weeks of gestational age groups received surfactant via the LISA technique, the overall distribution of gestational age between the two groups was comparable.

Statistical analysis using the chi-squared test ( $\chi^2 = 4.6$ ,  $df = 2$ ,  $p = 0.10$ ) demonstrated no statistically significant association between gestational age and the choice of surfactant administration method. Hence, it can be inferred that the gestational age of the neonates had no bearing on the decision making to administer the surfactant by INSURE or LISA technique.

**Table no 2. Influence of Birth Weight on Method of Surfactant Administration**

Birth Wight->	Less than 1000 grams	1000 – 1500 grams	More than 1000 grams
INSURE [n, (%)]	16(17.7%)	18(20%)	8(8.8%)
LISA [n, (%)]	12(13.3%)	22(24.4%)	14(15.5%)
Total [n, (%)]	28(31.1%)	40(44.4%)	22(24.4%)

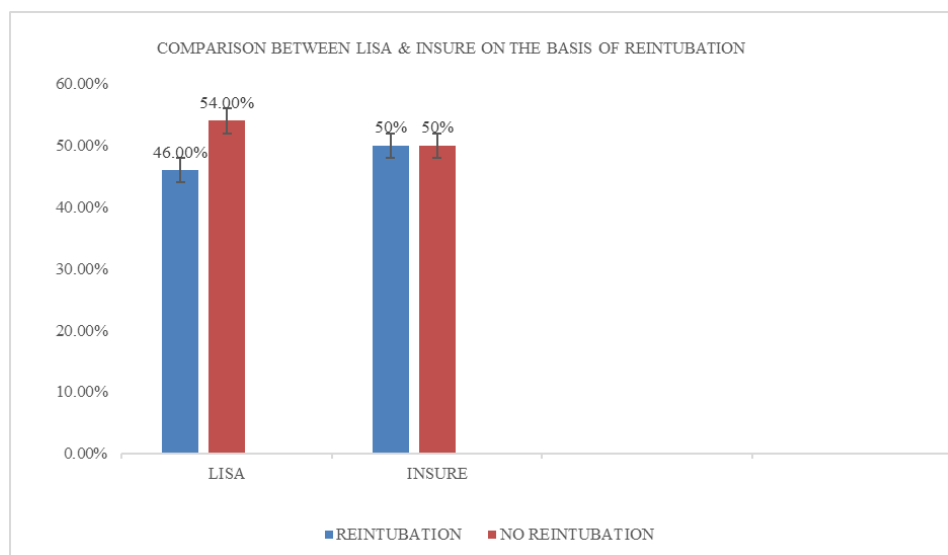
**Table no 2**, Shows the distribution of neonates by birth weight according to the method of surfactant administration (INSURE versus LISA)

There was no statistically significant association between birth weight and the method of surfactant administration ( $\chi^2 = 5.1$ ,  $df = 2$ ,  $p = 0.082$ ). Hence, the method of surfactant administration was not influenced by the birth weight of the neonates.

**Table no 3. Requirement of reintubation within 72 Hours**

	Reintubation	No reintubation	Total
INSURE (n, %)	20(50%)	20(50%)	40(44.4%)
LISA (n, %)	23(46%)	27(54%)	50(55.6%)
Total (n, %)	43(47.8%)	47(52.2%)	90(100%)

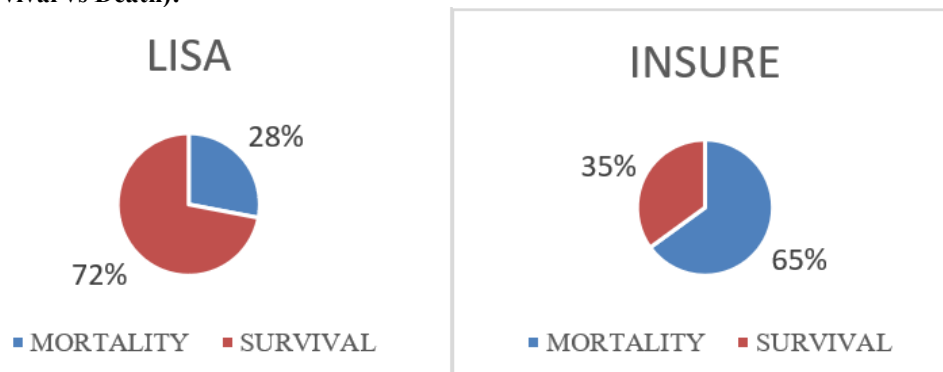
**Table no 3**, Shows the requirement of reintubation within 72 hours among neonates receiving surfactant by INSURE and LISA techniques.



**Figure no 2**, Shows the percentage wise distribution of preterm neonates who required reintubation within 72 hours among preterm neonates receiving surfactant by INSURE and LISA techniques.

44.4 % neonates in the INSURE group and 55.6% in the LISA group required re-intubation. However there was no statistically significant difference in the reintubation requirement between the two groups ( $\chi^2 = 0.143$ ,  $df = 1$ ,  $p = 0.705$ ).

**Outcome (Survival vs Death):**



**Figure no 3,** Shows the percentage distribution of preterm neonates who received surfactant by INSURE and LISA techniques on the basis of their survival outcome.

LISA group was associated with significantly higher survival, whereas INSURE group had a higher mortality rate ( $\chi^2 = 12.32$ ,  $df = 1$ ,  $p = 0.00044$ ).

#### IV. Discussion

In this retrospective observational study, we compared the outcomes of two surfactant administration techniques—INSURE and LISA—in preterm neonates with respiratory distress syndrome. Our findings demonstrate that while the requirement for reintubation within 72 hours was comparable between the two groups, mortality was significantly lower among neonates who received surfactant via the LISA technique.

Gestational age and birth weight did not significantly influence the choice of surfactant administration method in our cohort, suggesting that both techniques were applied across a similar clinical spectrum. This minimizes selection bias and strengthens the validity of the observed outcome differences.

The lack of a significant difference in reintubation rates between INSURE and LISA is consistent with previous studies, which have shown comparable short-term respiratory stability between the two techniques [7, 8]. This finding supports the safety of LISA and indicates that avoiding routine intubation does not increase the risk of early respiratory failure.

A key observation in our study was the significantly lower mortality in the LISA group. This benefit may be explained by reduced exposure to mechanical ventilation and preservation of spontaneous breathing, which together limit ventilator-induced lung injury and systemic inflammation [6, 9]. These mechanisms are believed to contribute to improved pulmonary and overall outcomes in preterm infants.

Our results align with earlier reports by Kribs et al., who first described improved survival with less invasive surfactant administration, as well as with subsequent observational studies and meta-analyses demonstrating reduced mortality and bronchopulmonary dysplasia rates with LISA [6,7,10]. Similar findings have been reported by Kaniewska and Gulczyńska and by Halim et al., further supporting the growing preference for LISA in neonatal practice [8, 11].

The limitations of this study include its retrospective design and single-centre setting, which may limit generalizability. Additionally, long-term outcomes such as bronchopulmonary dysplasia, duration of respiratory support, and neurodevelopmental follow-up were not evaluated. Despite these limitations, the study provides valuable real-world evidence supporting LISA as an effective and safe technique for surfactant administration in preterm neonates.

#### V. Conclusion

This study demonstrates that Less Invasive Surfactant Administration (LISA) is associated with significantly lower mortality compared with the conventional INSURE technique in preterm neonates with respiratory distress syndrome. The requirement for reintubation within 72 hours was comparable between the two methods, indicating that LISA does not compromise short-term respiratory stability.

The findings support the use of LISA as a lung-protective strategy that preserves spontaneous breathing and minimizes exposure to mechanical ventilation, thereby potentially reducing ventilator-associated lung injury. Given its favorable survival outcomes and comparable safety profile, LISA should be considered the preferred method of surfactant administration in appropriately selected preterm infants.

Further prospective, multicentric studies with long-term follow-up are recommended to evaluate additional outcomes such as bronchopulmonary dysplasia, duration of respiratory support, and neurodevelopmental outcomes.

### References

- [1]. Avery ME, Mead J. Surface Properties In Relation To Atelectasis And Hyaline Membrane Disease. *Am J Dis Child*. 1959;97:517–523.
- [2]. Sweet DG, Carnielli V, Greisen G, Et Al. European Consensus Guidelines On The Management Of Respiratory Distress Syndrome. *Neonatology*. 2019;115:432–450.
- [3]. Halliday HL. Surfactants: Past, Present And Future. *J Perinatol*. 2008;28:S47–S56.
- [4]. Jobe AH, Bancalari E. Bronchopulmonary Dysplasia. *Am J Respir Crit Care Med*. 2001;163:1723–1729.
- [5]. SUPPORT Study Group Of The Eunice Kennedy Shriver NICHD Neonatal Research Network. Early CPAP Versus Surfactant In Extremely Preterm Infants. *N Engl J Med*. 2010;362:1970–1979.
- [6]. Kribs A, Pillekamp F, Hünseler C, Et Al. Early Administration Of Surfactant In Spontaneous Breathing With Ncpap. *Neonatology*. 2008;93:288–294.
- [7]. Isayama T, Iwami H, McDonald S, Beyene J. Association Of Noninvasive Ventilation Strategies With Mortality And Bronchopulmonary Dysplasia. *JAMA*. 2016;316:611–624.
- [8]. Kaniewska U, Gulczyńska E. Influence Of LISA Vs INSURE On Outcomes Of RDS Treatment. *Dev Period Med*. 2019;23(3):163–171.
- [9]. Verder H, Robertson B, Greisen G, Et Al. Surfactant Therapy And Spontaneous Breathing. *Pediatrics*. 1994;94:135–139.
- [10]. Aldana-Aguirre JC, Pinto M, Featherstone RM, Kumar M. Less Invasive Surfactant Administration Versus INSURE. *Arch Dis Child Fetal Neonatal Ed*. 2017;102:F17–F23.
- [11]. Halim A, Shirazi H, Riaz S, Gul SS, Ali W. Less Invasive Surfactant Administration In Preterm Infants. *J Coll Physicians Surg Pak*. 2019;29(3):226–230.