



## EFFICACY OF SURFACTANT ADMINISTRATION VIA MIST TECHNIQUE VERSUS INSURE TECHNIQUE IN PRETERMS <37WKS WITH RESPIRATORY DISTRESS SYNDROME

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### ABSTRACT

**Introduction:** Neonatal respiratory distress syndrome (RDS) refers to the insufficiency of the lungs. INSURE approach, named after the key three stages in the procedure: INTubation, SURfactant administration and then Extubation as quickly as possible after administration. Minimally invasive surfactant therapy (MIST) administers surfactant into the trachea by direct laryngoscopy.

**Aim:** To measure the outcome of preterm infants (24-36wks) born with RDS who receives surfactant therapy via MIST technique versus INSURE technique.

**Materials and methods:** A detailed history and examination, procedure was done under aseptic precaution. The MIST method includes tracheal catheterization, intrapharyngeal instillation, and aerosolization. In this study, we will use a 4 to 5 FG (French Gauge) gastric tube as a conduit for insertion into the airway.

**Results:** In our study, all neonates included were born preterm, with an average gestational age of  $31.93 \pm 2.57$  weeks in the INSURE group and  $32.07 \pm 2.12$  weeks in the MIST group. The mean APGAR scores at 1 minute and 5 minutes exhibited close similarity between both groups. Instances of early onset sepsis, necrotizing enterocolitis, intraventricular hemorrhage, and pulmonary hemorrhage were noted in some neonates within both study groups. **Conclusion:** Surfactant administration for premature infants is vital important to prevent mortality and complications secondary to RDS. Conventionally minimally invasive techniques have less complications when compared to invasive method. But in resource limited settings one can consider both techniques as it has similar outcome with noninvasive one.

### INTRODUCTION:

Neonatal respiratory distress syndrome (RDS) refers to the insufficiency of the lungs that leads to certain signs, such as tachypnoea, cyanosis, retraction, and grunting at birth or shortly thereafter. RDS is the most important cause of morbidity and mortality in premature infants. The basis of RDS

treatment is respiratory support and surfactant replacement therapy. The early use of nasal continuous positive airway pressure (NCPAP) and administration of surfactant reduce the need for mechanical ventilation and its complications. Surfactant reduces the incidence of pneumothorax, pulmonary interstitial emphysema, chronic pulmonary disease, and death in the first 28 days of life.<sup>2</sup> Neonatal units are increasingly adopting a gentle approach to ventilator support in preterm infants as standard care. INSURE approach, named after the key three stages in the procedure: INTubation, SURfactant administration and then Extubation as quickly as possible after administration. This new technique aimed to avoid mechanical ventilation and intubation in infants who were initially managed with nasal continuous positive pressure (nCPAP). INSURE has been widely used since its introduction and has been shown to reduce both the need for mechanical ventilation and the incidence of chronic lung disease. However, the INSURE technique requires intubation of the trachea, positive pressure ventilation and sedation, and a number of negative side effects have been associated with the technique.<sup>5</sup>

Minimally invasive surfactant therapy (MIST) administers surfactant into the trachea by direct laryngoscopy, via a thin tube with the aid of Magill forceps, while the infant is supported with nCPAP. After surfactant instillation, the tube is immediately removed. MIST can avoid the need for sedation and tracheal intubation and has been shown to reduce the need for mechanical ventilation.<sup>5</sup>

The aim of this study is to measure the outcome of preterm infants (24-36wks) born with RDS who receives surfactant therapy via MIST technique versus INSURE technique.

This study was prospective observational study. The study was conducted at NICU of our hospital in Mysuru, a teaching tertiary care hospital attached to our Institute. Preterm newborns with respiratory distress syndrome formed the study subject. The study was conducted over a period of 12 months. This study included all preterm neonates (24-36wks) with RDS admitted in NICU, Cheluvamba Hospital Mysore. This study excluded Term neonates >37 weeks, Neonates associated with birth asphyxia, meconium aspiration syndrome, Neonates with congenital Anomalies and Neonates with congenital heart disease.

## METHODOLOGY

After obtaining approval by the institutional ethical committee and informed consent from parents/caregivers of the participants, detailed history and examination, procedure was done under aseptic precaution. The MIST method includes tracheal catheterization, intrapharyngeal instillation, and aerosolization. In this study, we will use a 4 to 5 FG (French Gauge) gastric tube as a conduit for insertion into the airway. The procedure involves checking the vocal cords using laryngoscopy, insertion of the gastric tube into the airway using Magill forceps, and administration of the surfactant (Neosurf 5ml/kg).

In InSurE technique the infant will be first intubated with an endotracheal tube appropriate to his weight and gestational age. A 5ml/kg dose of surfactant (Neosurf) will be administered by a feeding tube passed through the tracheal tube over 1 - 3 minutes, during which positive pressure ventilation will be applied by a self-inflating bag and the infant was then extubated and placed on nasal CPAP once again. After 12 hours, if FiO<sub>2</sub> > 40% was still required to maintain O<sub>2</sub> saturation within the range of 85% - 95%, the second dose of surfactant will be administered. This is a prospective study which will be done between two groups of newborns those received surfactant through MIST and those by InSurE techniques. Before administration of surfactant each baby will be allocated to either of 2 groups by simple randomization the procedure is selected and outcome symptoms are evaluated.

## Statistical Analysis

All statistical methods for inferential study chi-square test, t test for independent samples, ROC curve shall be carried through SPSS for windows (version 20) shall be expressed as mean, SD, frequency, percent. A p value of <0.05 shall be considered as significant. Purposive sampling method was used. A minimum sample size of 60 preterm neonates with RDS shall be taken up for

the study which calculated based on the prevalence of 4% of neonatal mortality due to RDS amongst neonates attending our Hospital, at 0.05 significance level using the formula, sample size =  $Z^2pq/d^2$ , where  $Z= 1.96$ ,  $p$  is the prevalence of disease,  $d=96\%$  confidence interval,  $q= 1-p$ .

## RESULTS:

In our study, all neonates included were born preterm, with an average gestational age of  $31.93 \pm 2.57$  weeks in the INSURE group and  $32.07 \pm 2.12$  weeks in the MIST group. These values were closely aligned, showing no statistically significant difference. The predominant mode of delivery was normal vaginal delivery, and there was an even distribution of gender in both groups. However, the mean birth weight of neonates in the INSURE group was  $1663.33 \pm 470.31$  g, which was notably higher than the mean of  $1435.33 \pm 405.36$  g in the MIST group, and this difference was statistically significant. (Table 1)

**Table 1: Comparison of basic details of the delivery**

Subjects (N=60)		Surfactant		p-value
		INSURE (N=30)	MIST (N=30)	
Gestational Age (in weeks)		$31.93 \pm 2.57$	$32.07 \pm 2.12$	0.827
Mode of Delivery	Vaginal	27 (90.0%)	25 (83.3%)	0.448
	Cesarean	3 (10.0%)	5 (16.7%)	
Gender	Male	17 (56.7%)	17 (56.7%)	1.000
	Female	13 (43.3%)	13 (43.3%)	
Birth Weight (in grams)		$1663.33 \pm 470.31$	$1435.33 \pm 405.36$	0.049*

Our study focused on comparing primary outcomes across the groups. Specifically, the mean APGAR scores at 1 minute and 5 minutes exhibited close similarity between both groups. The proportion of neonates requiring intubation was comparable in both groups. Furthermore, the mortality rates were in closer ranges, with 43.3% in the INSURE group and 40.0% in the MIST group. None of these comparisons revealed statistically significant differences between the groups, indicating analogous outcomes in both cohorts. (Table 2)

**Table 2: Comparison of primary outcomes of the study**

Subjects (N=60)		Surfactant		p-value
		INSURE (N=30)	MIST (N=30)	
APGAR	At 1 minute	$6.80 \pm 0.55$	$6.57 \pm 0.63$	0.131
	At 5 minutes	$8.60 \pm 0.62$	$8.57 \pm 0.63$	0.837
Intubation	Yes	9 (30.0%)	10 (33.3%)	0.781
	No	21 (70.0%)	20 (66.7%)	
Outcome	Alive	17 (56.7%)	18 (60.0%)	0.793
	Death	13 (43.3%)	12 (40.0%)	

Further secondary outcomes were assessed across the groups. Comparable proportions were observed in both groups regarding mothers necessitating antenatal steroids and neonates requiring continuous PAP. The durations, including the time between birth and surfactant administration, as well as the length of stay in the NICU, did not exhibit statistically significant differences between the groups. These findings affirm the comparable performance of both surfactants, as evidenced by the similarity in secondary (Table 3)

**Table 3: Comparison of secondary outcomes of the study**

Subjects (N=60)		Surfactant		p-value
		INSURE (N=30)	MIST (N=30)	
<b>Antenatal Steroid</b>	Yes	23 (76.7%)	28 (93.3%)	0.071
	No	7 (23.3%)	2 (6.7%)	
<b>Continuous PAP</b>	Yes	22 (73.3%)	24 (80.0%)	0.542
	No	8 (26.7%)	6 (20.0%)	
<b>Birth to surfactant (in hours)</b>		5.40 ± 2.82	4.17 ± 1.98	0.055
<b>NICU Stay (in days)</b>		10.63 ± 8.04	11.50 ± 7.23	0.662

All the neonates in our study were systematically monitored for the occurrence of complications. Instances of early onset sepsis, necrotizing enterocolitis, intraventricular hemorrhage, and pulmonary hemorrhage were noted in some neonates within both study groups. However, the prevalence of these complications did not exhibit statistically significant differences between the groups. (Table 4)

**Table 4: Comparison of complications among the subjects in the study**

Subjects (N=60)		Surfactant		p-value
		INSURE (N=30)	MIST (N=30)	
<b>Pneumothorax</b>	Yes	0 (0.0%)	0 (0.0%)	-
	No	30 (100.0%)	30 (100.0%)	
<b>Patent Ductus Arteriosus</b>	Yes	0 (0.0%)	0 (0.0%)	-
	No	30 (100.0%)	30 (100.0%)	
<b>Early Onset Sepsis</b>	Yes	20 (66.7%)	24 (80.0%)	0.542
	No	10 (33.3%)	6 (20.0%)	
<b>Necrotizing Enterocolitis</b>	Yes	1 (3.3%)	5 (16.7%)	0.781
	No	29 (96.7%)	25 (83.3%)	
<b>Intraventricular Hemorrhage</b>	Yes	4 (13.3%)	15 (50.0%)	0.793
	No	26 (86.7%)	15 (50.0%)	
<b>Bronchopulmonary Dysplasia</b>	Yes	0 (0.0%)	0 (0.0%)	-
	No	30 (100.0%)	30 (100.0%)	
<b>Pulmonary Hemorrhage</b>	Yes	5 (16.7%)	5 (16.7%)	1.000
	No	25 (83.3%)	25 (83.3%)	

## DISCUSSION:

Hyaline membrane disease (HMD) is the most common cause of respiratory distress in the preterm infants and most common cause for NICU admission. Respiratory distress syndrome/ HMD which occurs due to insufficient or decreased amount of surfactant production in the premature lung. Surfactant is a mixture of proteins and phospholipids that creates a cohesive surface layer over the alveoli which reduces the surface tension and maintains alveolar stability therefore preventing atelectasis during expiration. hence in premature infants with respiratory distress surfactant replacement is necessary to prevent complications. Surfactant replacement therapy (SRT) is very important in the management of neonates with respiratory distress syndrome (RDS) because it improves survival and reduces respiratory morbidities. Conventionally, the most common practice of administering surfactant to infant is a technique referred to as the INSURE method. This method involves an endotracheal intubation, providing a direct point of entry for surfactant to be instilled,

followed by extubation to a non-invasive positive pressure system. Newer methods of noninvasive surfactant administration, like MIST (minimally invasive surfactant therapy) or LISA (least invasive surfactant administration) methods others include nebulization, laryngeal mask, intrapharyngeal, and thin catheter administration as routes to introduce surfactant to the neonate these methods allow the patient to breath spontaneously while receiving surfactant, reducing the need for positive pressure ventilation and intubation. With the increasing use of noninvasive ventilation as the primary mode of respiratory support for preterm infants at delivery, prophylactic surfactant is no longer beneficial.<sup>3,7,8</sup> Both the INSURE and MIST methods are effective in improving end-expiratory lung volumes and compliance in premature infants with RDS, the complications associated with endotracheal intubation can diminish the benefits of surfactant replacement therapy.<sup>3</sup> However, both methods of surfactant administration have their own complications in terms of the patient, such as oxygen desaturation, bradycardia, and airway obstruction.<sup>9</sup>

In this study we have compared outcome between InSurE technique and minimally invasive technique. According to most of the study MIST technique followed by non invasive ventilation has better outcome when compared to InSurE technique alone.<sup>8,9</sup> In our study Even though complications following MIST technique is more when compared to InSurE as per results obtained there were no statistically significant difference in outcome between invasive and minimally invasive technique.

### Conclusion:

Surfactant administration for premature infants is vital important to prevent mortality and complications secondary to RDS. The method which is used to administer surfactant is also important for better outcome. Conventionally minimally invasive techniques have less complications when compared to invasive method. But in resource limited settings one can consider both techniques as it has similar outcome with noninvasive one. To provide recommendations regarding which method to follow for which severity of RDS need more studies.

### REFERENCES

- 1) Choupani R, Mashayekhy G, Hmidi M et al titled “Comparative Study of the Efficacy of Surfactant Administration through a Thin Intratracheal Catheter and its Administration via an Endotracheal Tube in Neonatal Respiratory Distress Syndrome”. Iranian Journal of Neonatology. 2018 Dec; 9(4). DOI: 10.22038/ijn.2018.30057.1408
- 2) Ziba Mosayebi, Maliheh Kadivar et al titled “A Randomized Trial Comparing Surfactant Administration Using InSurE Technique and the Minimally Invasive Surfactant Therapy in Preterm Infants (28 to 34Weeks of Gestation) with Respiratory Distress Syndrome”.J Compr Ped. 2017 November; 8(4):e60724. doi: 10.5812/compreped.60724.
- 3) Wang, X., Chen, L., Chen, S., Su, P., Chen, J. (2020). Minimally invasive surfactant therapy versus intubation for surfactant administration in very low birth weight infants with respiratory distress syndrome. *Pediatrics & Neonatology* 61(2), 210-215
- 4) Bhupendra Kumar Gupta, Anindya Kumar Saha et al, titled “Minimally invasive surfactant therapy versus InSurE in preterm neonates of 28 to 34 weeks with respiratory distress syndrome on non-invasive positive pressure ventilation—a randomized controlled trial”.European Journal of Pediatrics 2020 <https://doi.org/10.1007/s00431-020-03682-9>
- 5) Marta Aguar, Mar\_ia Cernada et al titled “ Minimally invasive surfactant therapy with a gastric tube is as effective as the intubation, surfactant, and extubation technique in preterm babies” DOI:10.1111/apa.12611, feb 2014
- 6) Moon Young Seo, Gyu Hong Shim et al titled “Clinical Outcomes of Minimally Invasive SurfactantTherapy via Tracheal Catheterization in Neonates with aGestational Age of 30 Weeks or More diagnosed with Respiratory Ditrress Syndrome” Neonatal Med 2018 August;25(3):109-117.

- 7) Ng EH, Shah V. Guidelines for surfactant replacement therapy in neonates. *Paediatr Child Health*. 2021 Feb 1;26(1):35-49. doi: 10.1093/pch/pxaa116. PMID: 33552321; PMCID: PMC7850281.
- 8) Riaz, M., Asmat, S., Shaukat, F., Aslam, M., Majeed, M., Rafiquq, S. (2019). Efficacy of surfactant administration to preterm infants via thin catheter versus INSURE technique. *The Professional Medical Journal* 27(2), 431-436. DOI: 10.29309/TPMJ/2020.27.2.4176.
- 9) Polin, R., Carlo, W. (2014). Surfactant replacement therapy for preterm and term neonates with respiratory distress. *Pediatrics* 133(1), 156-163.