

To Study the Influence of Technique of Surfactant Administration Lisa (Less Invasive Surfactant Administration) Vs. Insure (Intubate Surfactant Administration Extubate) on the Outcome of Respiratory Distress Syndrome Treatment in Preterm Infants (A Study of 100 Cases)

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Abstract: *The incidence of Respiratory Distress Syndrome due to surfactant deficiency in premature infants is 50% in gestational age of 26-28 weeks to 25% in 30-32 week GA. Exogenous surfactant administration is the standard of care in these patients. This study is an observational retrospective + prospective longitudinal study. 100 preterm infants hospitalized in neonatology department and administered surfactant by LISA and INSURE technique for RDS were enrolled in the study as per inclusion criteria. An observation of the vitals before and after the procedure, along with the time required to administer the surfactant as well as the primary and secondary outcomes in infant were recorded. Results were analysed with help of standard statistical tests. The mean change in respiratory rate, heart rate, O₂ saturation with LISA and INSURE were comparable. The mean procedural time with LISA was 8 ±2 min, whereas with INSURE being 16±2 min (Z test: p value=<0.001). The incidence of mechanical ventilation within 72hrs of surfactant administration with LISA was 16% whereas with INSURE being 30% (Chi-square test: p=0.096). The average duration of hospital stay was 8±2 days with LISA and 14±2 days with INSURE (Z test: p=<0.001; significant). The mortality rate in LISA was 16% and with INSURE 30% (Chi-square test: p=0.049).*

Keywords: surfactant therapy, RDS, LISA, INSURE

1. Introduction

Neonatal respiratory distress syndrome or RDS also known as Hyaline Membrane Disease or HMD is a common cause of respiratory distress in a newborn, presenting within hours, most often immediately after delivery. RDS primarily affects preterm and infrequently, term neonates. The incidence is inversely proportional to the gestational age of the infant, with more severe disease in smaller and premature neonates.

As the most common cause of respiratory distress in premature infants, the incidence of neonatal RDS ranges from 2.2% to 7.6% in developed countries and from 0.7% to 8.3% in India. Data shows occurrence of RDS in about 24,000 infants in the United States annually. The most important risk factors are prematurity and low birth weight. Others include male gender, late preterm delivery, maternal diabetes, perinatal hypoxia and ischemia and delivery in the absence of labour.[88]

In one study of babies born between 2003 and 2007 at various National Institute of Child Health and Human Development (NICHD) Neonatal Research Network centre, 98% of babies born at 24 weeks had RDS, while at 34 weeks, the incidence was 5% and at 37 weeks was less than 1%. [1]

HMD occurs when there is not enough of a substance in the lungs called surfactant. Surfactant is made by the cells in the airways and consists of phospholipids and protein. It begins to be produced in the fetus at about 24 to 28 weeks of pregnancy, and is found in amniotic fluid between 28 and 32 weeks. By about 35 weeks gestation, most babies have developed adequate amounts of surfactant; therefore infants born before this duration are susceptible to develop RDS.

Enormous strides have been made in understanding the pathophysiology and management of respiratory distress syndrome, leading to improvements in morbidity and mortality in infants with this condition.

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Advances include the following:

- The use of antenatal steroids to enhance pulmonary maturity
- Appropriate resuscitation facilitated by placental transfusion and immediate use of continuous positive airway pressure (CPAP) for alveolar recruitment
- Early administration of surfactant
- The use of gentler modes of ventilation, including early use of "bubble" nasal CPAP to minimize damage to the immature lungs.
- Supportive therapies, such as the diagnosis and management of patent ductus arteriosus, fluid and electrolyte management, trophic feeding and nutrition.

In the last 30 years surfactant replacement with exogenous surfactant preparations derived from animal sources became the most effective evidence-based therapy for RDS. The mode of administration has evolved especially in the last decade from endotracheal surfactant bolus administration during mechanical ventilation over Intubate-SURfactant-Extubate (INSURE) followed by continuous positive airway pressure (CPAP) towards less invasive techniques [less invasive surfactant administration (LISA), Minimal Invasive Surfactant Techniques(MIST)] that aim to effectively provide an adequate dose of surfactant while the infant is breathing spontaneously.

Aims and Objectives

- To compare the vitals of the patient before and after surfactant administration.
- To compare the time required to administer the surfactant with either technique.
- To compare the primary and secondary outcomes in the management of RDS after surfactant administration.

Primary outcome:

- 1) Mechanical ventilation <72 hours
- 2) Pneumothorax
- 3) Late onset sepsis
- 4) Apnea
- 5) Bradycardia
- 6) Surfactant reflux
- 7) Coughing/ gagging
- 8) Need for more than 1 dose of surfactant

Secondary outcome

- 1) Pulmonary hemorrhage
- 2) IVH \geq stage 2
- 3) PDA requiring treatment
- 4) ROP \geq stage 2
- 5) NEC \geq stage 2
- 6) Bronchopulmonary dysplasia
- 7) Length of NICU stay
- 8) Final outcome: Discharge/ Expired

2. Materials and Methods

This study is an observational retrospective + prospective longitudinal study. 100 preterm infants hospitalized in neonatology department and administered surfactant by LISA and INSURE technique for RDS were enrolled in the study as per inclusion criteria. An observation was made

regarding the changes in the vitals of the infant during the procedure, along with the time required to administer the surfactant as well as the primary and secondary outcomes in each infant. Results were analysed with help of standard statistical tests.

Rationale of study

Intubation/ventilation carries potential risks, including airway trauma due to direct instrumentation and ventilation induced lung injury from over distention of fragile preterm infant's lungs with intermittent positive airway pressure (IPPV). The use of anaesthetic drugs may also lead to prolongation of ventilation until baby starts breathing again.

To minimize these risks neonatologists and pediatricians can consider performing the less invasive surfactant administration (LISA) technique to administer rescue surfactant and benefit in terms of better survival, decreased need for mechanical ventilation and also reduced days of hospital stay.

3. Results

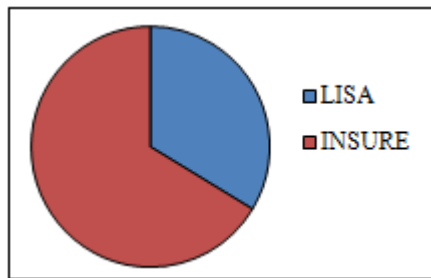
1) General Examination

	LISA		INSURE		p-value
	No.	%	No.	%	
Colour					
Pink	41	82	42	84	$\chi^2 = 0.07$
Peri cyanosis	9	18	8	16	$p = 0.96$
Central cyanosis	0	0	0	0	
Heart rate					
Pre-surfactant	151.4 \pm 13.39		155.64 \pm 9.38		Z = 1.834, p = 0.06
Post-surfactant	151.34 \pm 7.80		153.76 \pm 5.53		Z = 1.788, p = 0.07
Respiratory rate					
Pre-surfactant	58 \pm 8.02		59.56 \pm 4.75		Z = 1.183, p = 0.23
Post-surfactant	58.38 \pm 5.45		58.84 \pm 3.83		Z = 0.488, p = 0.62
spO₂	95.02 \pm 3.22		95.86 \pm 2.56		Z = 1.43, p = 0.15
Capillary refill time					
<3 sec	45	90	49	98	$\chi^2 = 2.83$ $p = 0.24$
3 sec	5	10	1	2	
>3 sec	0	0	0	0	

Thus comparing the general clinical parameters of both the study groups, there was a similar distribution with statistical tests showing no significant differences. Thus both the study groups are comparable and no major change in HR and RR of the patient was observed post surfactant administration.

2) Procedural Time

The mean procedural time for surfactant administration with INSURE technique was 16.68 \pm 1.82 seconds with statistically significant decrease in LISA technique to 8.48 \pm 1.42 seconds. [Z = 25.118, p = <0.0001]



Mean procedural time

3) Primary Outcome

	LISA		INSURE		p-value
	No.	%	No.	%	
Intubation <72 hours	8	16	12	24	$\chi^2 = 2.00$, p value = 0.15
Mechanical ventilation	8	16	12	24	$\chi^2 = 2.00$, p value = 0.15
Pneumothorax	2	4	3	6	$\chi^2 = 0.42$, p value = 0.51
Late onset sepsis	1	2	2	4	$\chi^2 = 0.68$, p value = 0.40
Apnea	1	2	1	2	$\chi^2 = 2.00$, p value = 0.15
Bradycardia	1	2	1	2	$\chi^2 = 0.00$, p value = 1
Surfactant reflux	6	12	4	8	$\chi^2 = 0.88$, p value = 0.34
Coughing/ gagging	8	16	2	4	$\chi^2 = 8.00$, p value = 0.004
Need for more than 1 dose of surfactant	3	6	1	2	$\chi^2 = 2.08$, p value = 0.14

In all of the above primary outcomes there was no significant difference in both the study group hence the change in technique of surfactant administration had no major impact in these outcomes.

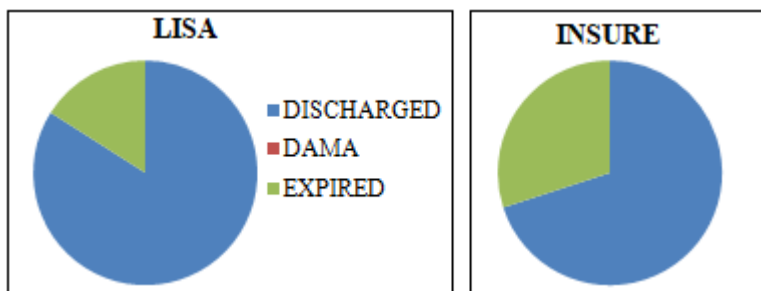
However the incidence of coughing or gagging during surfactant administration was found to be higher in LISA group (6%) compared to INSURE group (4%).

4) Secondary Outcome

	LISA		INSURE		p-value
	No.	%	No.	%	
Pulmonary hemorrhage	5	10	7	14	$\chi^2 = 0.75$, p = 0.38
IVH stage ≥ 2	1	2	1	2	$\chi^2 = 0.00$, p = 1
PDA requiring Rx	2	4	1	2	$\chi^2 = 0.68$, p = 0.40
ROP stage ≥ 2	1	2	2	4	$\chi^2 = 0.68$, p = 0.40
NEC stage ≥ 2	1	2	1	2	$\chi^2 = 0.00$, p = 1
Bronchopulmonary dysplasia	2	4	3	6	$\chi^2 = 0.42$, p = .51
Length of NICU stay(DAYS)	8.56		13.74		Z = 6.109, p = <0.0001
Final outcome					
Discharge	42	84	35	70	$\chi^2 = 5.53$, p = 0.01
Expired	8	16	15	30	$\chi^2 = 3.85$, p = 0.049
DAMA	0	0	0	0	

The technique of surfactant administration had no major impact on the incidence of pulmonary hemorrhage, IVH, PDA, ROP, NEC and BPD in these preterm infants post RDS treatment.

However, the mean duration of NICU stay was decreased in LISA group (8.56 days) compared to INSURE group (13.74 days). Also, the discharge rates were higher in LISA group(84%) compared to INSURE(70%) and the mortality rate lower in LISA(16%) compared to INSURE(30%).



4. Conclusions

- The time required to administer surfactant effectively was reduced with LISA technique.
- There was a significant reduction in the duration of hospital stay as well as mortality rate, with increase in the discharge rate of preterm infants.

References

[1] Smith PB, Ambalavanam N, Li L, Cotten CM, Laughon M, Walsh MC, Das A, Bell EF, Carlo WA, Stoll BJ, Shankaran S, Laptook AR, Higgins RD, Goldberg RN, Generic database subcommittee. Eunice Kennedy Shriver national institute of child health human development neonatal research network. Approach to

infants born at 22 to 24 weeks gestation: relationships to outcomes or more mature infants. Paediatrics. 2012 jun;129(6):e1508-16

[2] Aldana-Aguirre JC, Pinto M, Featherstone RM, Kumar M. Less invasive surfactant administration versus intubation for surfactant delivery in preterm infants with respiratory distress syndrome: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2017 Jan;102(1):F17-F23.

[3] Bugter IAL, Janssen LCE, Dielmen J, Kramer BW, Andriessen P, Niemarkt HJ. Introduction of less invasive surfactant administration (LISA), impact on diagnostic and therapeutic procedures in early life: a historical cohort study. BMC Pediatr.2020;20(1)1-9

[4] Mehler K, Broer A, Roll C, Gopel W, Weig C, Jahn P, et al. Developmental outcome of extremely preterm

infants is improved after less invasive surfactant
application: Developmental outcome after LISA. Acta
Paediatr Int J Paediatr.2020;(00):1-8