Surfactant Administration in Preterm babies (28-36 weeks) with Respiratory Distress Syndrome: LISA vs InSurE, an Open-Label Randomized Controlled Trial

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Abstract

ABSTRACT INtubation- SURfactant-Extubation (InSurE) approach is traditional method of surfactant delivery in preterm neonates with Respiratory Distress Syndrome (RDS). Newer, Less Invasive Surfactant Administration(LISA) techniques lessen the need for mechanical ventilation and its adverse consequences. Evidence on the favourable effects of LISA can't be extrapolated from developed to developing countries. Aim of Study is to compare the effectiveness of InSurE and LISA. **Objectives:** Primary outcome was to find need of intubation and mechanical ventilation within 72 hrs of birth. Neonates were followed until discharge/death for adverse events and complications. **Material & Methods**: Open-label RCT was conducted at tertiary neonatal intensive care unit. Preterm neonates with diagnosis of RDS were randomized in two groups (InSurE or LISA) to receive surfactant soon after birth. **Results:** Total of 150 neonates were analysed (75 in each group). Insignificant Statistical difference was seen in the need for intubation and mechanical ventilation within 72 h of birth between the two groups [InSurE, 30 (40%) and LISA, 30(40%), relative risk 1.0, 95% confidence interval 0.68–1.48]. 12% (n=9, LISA group) & 14.6% (n=11 InSurE group) had adverse events during the procedure. Also, we observed insignificant statistical difference in the rates of major complications or duration of respiratory support, hospital stay & mortality. **Conclusion**: : LISA and InSurE are equally effective for surfactant administration in the treatment of RDS, when NIPPV is the primary mode of respiratory support. More RCTs are required to compare the efficacy & long-term outcomes of LISA with InSurE. Keywords- Intubation, Mechanical Ventilation, NIPPV.

INTRODUCTION

Respiratory distress syndrome (RDS), one of the most common respiratory illness in preterm infants, is mainly due to the lack of pulmonary surfactant, leading to atelectasis, ventilation-perfusion (V/Q) mismatch, and often resulting in neonatal morbidity and mortality (1,2). Since the early 1990s, Surfactant replacement therapy (SRT) for RDS has been a standard of care across neonatal intensive care units (NICU) (3). Along with invasive ventilation, it plays a vital role in the pathophysiology of bronchopulmonary dysplasia (BPD), which remains common morbidity in preterm neonates (4,5). Nasal continuous positive airway pressure (nCPAP) is frequently used for RDS to decrease the incidence of acute lung injury. The combination of Surfactant therapy with nCPAP for alveolar recruitment has transformed the management of RDS(6). The classical InSurE technique introduced by Verder et al. (1990) involving Intubation, Surfactant administration with brief positive pressure ventilation, and Extubation, along with nCPAP has been the standard of care for RDS(7). To avoid intubation for delivering surfactant in preterm infants with RDS, less invasive surfactant administration (LISA) ,also known as minimally invasive surfactant therapy (MIST) techniques have been described (8–10). LISA came into focus by attaining surfactant delivery while maintaining spontaneous breathing and avoiding the need for endotracheal tube intubation even for a split second(11). LISA technique has been suggested as the preferred way of surfactant administration to preterm infants with RDS as an alternative to InSurE(12–14).

nCPAP has been a part of the standard of care in managing preterms with RDS. Although it reduces the need for invasive mechanical ventilation(IMV), there is substantial evidence of nCPAP failure as high as 35-50%(6,15,16). Hence, nasal intermittent positive pressure ventilation (NIPPV) can be a better option as it delivers time cycled peak inspiratory pressure (PIP) above Positive End Expiratory Pressure (PEEP), thereby delivering higher mean airway pressure at nasal interface compared to nCPAP(17). Evidence from the literature suggests that NIPPV as primary mode of respiratory support has lower rates of failure and need for IMV(18–21).

There is limited data about the feasibility and efficacy of LISA from developing countries. Moreover, hardly very few RCTs have been published comparing LISA vs InSurE using NIPPV as a primary mode of respiratory support. This prospective open-label RCT was planned to study the comparative efficacy of LISA with InSurE in preterm (28-36 weeks of gestation) with RDS using NIPPV as a primary mode of respiratory support.

The primary objective was to find need of intubation and mechanical ventilation within 72 hrs of birth. Neonates were followed until discharge/death for adverse events and complications.

MATERIAL AND METHODS

This prospective, single-centre, open-label, randomized controlled trial was conducted in neonatal intensive care unit (NICU, Level 3) at tertiary care teaching hospital in western India.

Inclusion Criteria: Spontaneously breathing preterm neonates between 28 to 36 weeks of gestation diaginosed with RDS were enrolled in the study.

Exclusion Criteria: newborns with a major congenital malformation (congenital heart disease, congenital diaphragmatic hernia, tracheoesophageal fistula, choanal atresia, cleft palate, malformation of the upper airway, Pierre-Robin sequence *etc*) severe perinatal asphyxia requiring PPV or poor respiratory effort requiring intubation in the delivery room were excluded from the study.

Sample size: One previous study(22) showed, 40% of infants in InSurE group required intubation in the first 72 h of life. To decrease the need of IMV with LISA to 20% (Power of 80 percent and alpha error of 0.05) we estimated a sample size of 75 in each group. Data analysis was done by using SPSS software version 19. qualitative data were expressed as frequency/ percentage. Quantitative data was stated as mean (S.D) and median (IQR). Chi-square test and Fisher's exact test were used to compare qualitative variables. Z test and Mann-Whitney U test were used for quantitative variables. P value < 0.05 was considered significant.

Institutional ethics committee (IEC) approval was taken and written informed consent was taken from the parents before the procedure. Written informed consent was taken from the parents before the procedure at the time of enrollment before randomization. Trial registered with Clinical Trial Registry India (CTRI/2022/01/039147).

Study protocol: RDS was diagnosed clinically in preterm babies based on the need for supplemental oxygen or respiratory support, clinical signs of tachypnea, retractions, grunting, and,or chest x-ray suggestive of RDS (low volume lung, bilateral reticulogranular pattern) in the initial hours of life. Premies with RDS were initially stabilized, and put on respiratory support in the form of NIPPV with initial settings of PIP 15-16 cm of H2O, PEEP of 6-8 cm of H2O, rate of 40 min, and FiO2 [Oxygen fraction in inspired air] adjusted to achieve a target saturation of 90 to 95% with use of the Sophie (Fritz Stephan GMBH, Germany) or Fabian (Acutronic Medical System, Switzerland) ventilator. Snugly fitting appropriate size binasal prongs were used as the interface for NIPPV. Surfactant was given after randomization by either LISA or InSurE technique to patients requiring FiO2 of more than 30% and PEEP more than 6cm of H2O to maintain target saturation of 90-95%(14).

No premedication was used in either group. Non-pharmacological measures like swaddling and nesting were done to comfort the baby during the procedures. Repeat surfactant was given after 6-12 hours by the same technique if the patient continued to have FiO2 requirement more than 30% with significant respiratory

distress. In either group, NIPPV failure was considered and infants were mechanically ventilated if they had any of the following: severe respiratory distress with SAS [?] 7, FiO2 requirement [?] 0.6 on NIPPV, Arterial blood pH <7.2, pCO2 [?] 60 mmHg, or significant apnea and hemodynamic instability. Weaning from NIPPV to O2 by NC was considered if the baby did not show any sign of respiratory distress or apnea for 24hrs with setting of PIP: 12-14cm of H2O, PEEP:4-5cm of H2O and FiO2 <30%.

The detail of each technique is described below:

LISA: The procedure was performed by two trained residents and a staff nurse for assistance. A sterile(gamma/ETO Sterilized) 5Fr (Single lumen, Infant feeding tube GS-4008-ROMSONS) feeding tube was used for delivering surfactant and desired tip to lip distance was decided as per nasotragal length plus 1 cm (NTL+1 cm). Surfactant (beractant) 100mg/kg was prefilled in a 5 to 10 ml syringe under aseptic precaution, and an additional 1 mL of air was drawn up, taking into consideration the dead volume of the tube. Direct laryngoscopy was performed and a feeding tube was inserted to the desired depth (1-2 cm below vocal cords) without using Magill forceps. After placing the tube, the laryngoscope was removed and surfactant was administered slowly over 60-120 seconds, and then the catheter was removed immediately. NIPPV was continued throughout the procedure. Patients were given manual breaths or PPV in case of apnea/bradycardia.

InSurE: Patients were intubated with an appropriate sized endotracheal tube (ETT) ,and surfactant was administered through a sterile 5Fr feeding tube passing through the ETT followed by PPV using an appropriately sized self-inflating resuscitation bag. Babies were extubated after a few minutes and continued on NIPPV support.

Randomization: Infants were randomly assigned to LISA and InSurE group with 1:1 allocation ratio using online computer-generated sequential random numbers, and concealment was done using serially numbered opaque sealed envelopes. Blinding was not done because of the nature of intervention in treatment groups.

Interventions: Asynchronised NIPPV was used as primary mode of respiratory support in both the groups. As servo-controlled oxygen delivery was not available, FiO2 was controlled manually. Aside from the experimental intervention, the groups recieved similar treatment.

The primary outcome of the study, was to evaluate the need for IMV (Invasive Mechanical Ventilation) within the first 72 hours of birth. Babies were followed until discharge/death for a secondary outcome which included intraventricular hemorrhage (IVH), hemodynamically significant patent ductus arteriosus (hsPDA), necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), and BPD. Also, duration of invasive ventilation, non invasive respiratory support, oxygen by nasal cannula, need for repeat surfactant doses, length of hospital stay, and adverse events during surfactant administration were recorded. For diagnosing IVH, cranial ultrasound was performed first within 48-72 hours, and then on day7 and 14 of birth. The diagnosis of BPD referred to the requirement of respiratory support at 36 weeks of gestation(23).

Fig. 1 CONSORT flow chart

RESULTS

A total of 150 neonates were randomized to one of the two groups of LISA and InSurE (Fig. 1). Baseline characteristics were comparable in both groups (Table 1). The mean gestational Age was 31.4 weeks (±0.53 SD), whereas the mean birth weight of the population was 1243.94g (± 212.60 SD). All the babies were followed till discharge/death. Table.2 depict Primary and secondary outcomes. We observed statistically insignificant difference in the need for intubation within 72 h of birth between the InSurE and LISA group [Relative Risk(RR) of 1.0, 95% of Confidence Interval(CI) 0.68–1.47).Complications like IVH, hsPDA, Pneumothorax, BPD, LOS, NEC, and ROP were more in the InSurE group, however, the difference was statistically insignificant. There was no difference in requirement of the second dose of surfactant between two groups. Also, difference was statistically insignificant in the duration of need for NIPPV,mechanical ventilation and supplemental oxygen. Adverse events during the procedure such as transient desaturation/bradycardia were

more in the InSurE group but the P-value was not significant. Furthermore, insignificant statistical difference was seen in the duration of hospital stay and survival outcome among the two groups.

TABLE -1.Baseline characteristics of study groups

Indicators	LISA (n=75)	InSURE (n=75)	P-value
Gestational Age (weeks), Mean ± SD	31.41±0.30	31.36 ± 0.69	0.57*
Gestational age group			
28 to < 32 weeks, n (%)	49	50	0.90**
32 to < 34 weeks, n (%)	23	23	
[?] 34 weeks, n (%)	03	02	
SGA n (%)	32	35	0.74***
AGA n (%)	43	40	
LGA n (%)	00	00	
Birth weight, g, Mean ± SD	1226 (±176)	1261.5 (±244)	0.30*
Birth weight group			
ELBW (<1000 g)	08	09	0.49**
VLBW (1000–1499 g)	59	62	
LBW (1500–2499 g)	08	04	
Gender			
Male, n (%)	39	41	0.87***
Female, n (%)	36	34	
APGAR Score, Median (IQR)			
1 min	5(4-6)	5(5-6)	0.25#
5 min	7(7-8)	8(7-8)	0.56#
Mode of delivery			
Vaginal, n (%)	55(73.33%)	52(69.33%)	0.71***
Caesarean, n (%)	20(26.66%)	23(30.66%)	
Antenatal steroids			
Complete course, n (%)	22 (29.33%)	21 (28 %)	0.98**
Incomplete course, n (%)	37 (49.33%)	38(50.66%)	
Not received, n (%)	16(21.33%)	16(21.33%)	
Antenatal complications			
GDM, n (%)	03	02	0.97**
PIH	29	32	
ECLAMPSIA	05	04	
APH	16	15	
PPROM	24	22	
MAX PEEP before surfactant, Median (IQR)	7 (6-7)	7 (6-7)	0.87#
Age at surfactant therapy (hrs), Mean ± SD	2.98 ± 0.70	2.8 ± 0.79	0.13*

Indicators	LISA (n=75)	InSURE (n=75)	P-value
SAS Score before surfactant, Median (IQR)	5(5-6)	5 (5-6)	0.89#

InSurE, intubate-surfactant-extubate; LISA, less invasive surfactant administration; n, number; g, grams; SD, standard deviation; ELBW, extremely low birth weight; VLBW, very low birth weight; LBW, low birth weight; SGA, small for gestational age; AGA, appropriate for gestational age; LGA, large for gestational age; PPROM preterm premature rupture of membrane; GDM gestational diabetes mellitus; APH antepartum hemorrhage; PIH pregnancy-induced hypertension; IQR, interquartile range.

*Z test.; ** Chi-Square Test ; ***Fisher's exact test; #Mann–Whitney U-test

TABLE -2. Outcome variables of the study group

Primary outcome	LISA (n=75)	InSURE (n=75)	RR (95% CI)	P-value
Intubation within 72h of birth, n (%)	30(40%)	30(40%)	1.0 (0.68 to 1.48)	>0.99***
Secondary outcomes (Major complications) n (%) ***CT***				
IVH	07	09	0.9418 (0.49 – 1.50)	>0.99***
BPD	06	09	0.85 (0.41 – 1.43)	0.79***
hsPDA	28	30	1.07 (0.75 – 1.47)	0.74***
NEC	03	04	0.92 (0.33 – 1.68)	>0.99***
Pneumothorax	01	02	0.50 (0.04 – 5.40)	0.99***
LOS	27	30	1.038 (0.72 – 1.43)	0.87***
ROP	08	10	0.96 (0.51 – 1.49)	>0.99***
Median (IQR) duration of MV (days)	6.5 (5.5-7)	6.25 (5.5-7)	–	0.40#
Median (IQR) duration of non-invasive respiratory support (days)	6 (5-6)	6(5.25-6.5)	–	0.50#
Median (IQR) Duration of Supplemental Oxygen	5(3-11)	5(3-14)	–	0.90#
Repeat dose of surfactant, n (%)	13 (17.33%)	11 (14.66%)	–	0.82**
Adverse events during surfactant administration				
Transient desaturation/ bradycardia), n (%)	9 (12%)	11 (14.66%)	–	0.63**

Primary outcome	LISA (n=75)	InSURE (n=75)	RR (95% CI)	P-value
Regurgitation, n (%)	4 (5.33%)	3 (4%)	–	0.69**
Median (IQR) length of hospital stay (days)	30.5(22-39)	26 (18.5-41)	–	0.56#
Survival n (%)	54 (72%)	52 (69.33%)	1.07 (0.76 -1.57)	0.86***

InSurE, intubate-surfactant-extubate; LISA, less invasive surfactant administration; RR, relative risk; 95% CI, 95% confidence interval; n, number; IVH, intraventricular hemorrhage; BPD, bronchopulmonary dysplasia; hsPDA, hemodynamically significant patent ductus arteriosus; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; d, days; IQR, interquartile range.

** Chi-Square Test test; ***Fisher's exact test.; #Mann–Whitney U-test

DISCUSSION

In this open-label RCT, we compared the newer less invasive surfactant administration technique with the traditional, more invasive method of surfactant instillation, InSurE. The population included spontaneously breathing preterm babies between 28 to 34 weeks of gestation with RDS using NIPPV as a primary mode of ventilation. A less invasive approach was proven to be equally effective with no significant difference in the need for mechanical ventilation within 72hours of birth between the two groups. We found insignificant statistical difference in duration of ventilation, oxygen therapy, length of hospital stay, major complications, adverse events, or mortality between the two groups.

InSurE has been the traditional method of surfactant administration. However, a brief period of invasive ventilation in this technique may also cause lung injury, so less invasive methods (LISA) came into the field. Following an initial pilot trial by Verder et al.(24), several variations have been conducted and published over years using different types of catheters for intratracheal administration of surfactant with or without Magill forceps(25–28). Over the years LISA has been increasingly used in different parts of the world. Few studies have been reported from India.

As with our study, several other trials(27–34) found no significant difference between the InSurE and LISA groups about the need for intubation within 72 hours of birth. Mohammadizadeh, et al.(28) Conducted a multicentre RCT in Iran among 38 preterm babies below 34 weeks gestational age and found insignificant difference in the need for intubation within first 72 hours of life. Similar findings were seen in a single-centre RCT from china by Bao et al(27). However, various studies(22,31,35,36) of similar design and meta-analysis(1,4,37,38) from various countries in the world have reported a significant reduction in the need for mechanical ventilation in the LISA group. Most of studies(22,31,35,36) which found significant difference in the need of MV in 72 h used nCPAP as their primary respiratory support. Evidence from literature shows that NIPPV facilates better deliver of presure in the alveoli to overcome the airway clog and leaks during catheterisation by a thin intra-tracheal catheter(39). Also NIPPV prevents intubation(18). Both these factors may explain the lack of difference between LISA and InSurE groups in the primary outcome in our study.

In our study, we used NIPPV as a primary mode of respiratory support whereas the majority of the studies which found a significant difference in the need for intubation in the first 72h used nCPAP as their primary mode of ventilation(2,31,35,36). Evidence from the literature supports that NIPPV as the primary mode of respiratory support reduces the need for mechanical ventilation(18). Multiple studies(17,40) and meta-analysis (40,41) suggest that NIPPV works better than CPAP in reducing the need for mechanical ventilation. The possible mechanism explained is the inclusion of PIP above PEEP, thereby delivering higher MAP, improving alveolar recruitment, and thus reducing the work of breathing(17,40–43). This can explain the lack of difference in the primary outcome among both the groups in our study. Other notable Indian

research by Gupta et al.(29) and Pareek et al.(34) using NIPPV showed no significant difference in the need for intubation within the first 72h. Similar findings were seen in a recent trial from Turkey by Akcay et al.(30)

The study population included preterm babies of a wider gestational age range (28-36weeks) with a mean gestational age of 31.4 weeks. It is comparable with other studies(29,34). Most of the studies have included preterms below 34 weeks of gestation(27,28,30,32,35,36,44). It is uncertain whether difference in the study groups affected key endpoints. There were insignificant statistical difference in the duration of MV/ NIPPV or supplemental oxygen and the incidence of BPD between the groups.This could be attributed to similar rate of mechanical ventilation in both the groups. Similar findings were reported from other studies(27–30,33,34). We found no significant difference in other major complications such as IVH, NEC, ROP, hsPDA, pneumothorax, and LOS between the groups. Similar results were reported from other studies(27,29,30,34,44). Our study did not show any significant difference between the groups in the need for a second dose of surfactant, as did most of the studies of similar design(27,29,34,36). Continuous NIPPV support along with LISA gives a better pressure effect(45), potential reason for less surfactant retreatment in our study. There was no substantial difference in the rate of adverse events such as transient bradycardia/desaturation during the procedure(12% LISA &14.6% InSurE, p = 0.63), comparable with other studies(27,29,36). In contrast, Olivier et al(46) and Mohamadizadeh et al.(28) reported a statistically significant higher incidence of desaturation/ bradycardia during the procedure, attributed to premedication for sedation before the procedure or inadequate training. Duration of hospital stay was also similar among the groups, comparable to other studies(2,27,33). There was no statistically significant difference in the survival outcome between the groups (RR: 1.06, 95%CI:0.76-1.57 (37,47). Gestational age stratified subgroup analysis was done for all primary and secondary outcomes and findings did not differ from main results..

Generalizability of the study: this study can be replicated in tertiary level nicu of many LMICs, provided NIPPV facility should be available

Strength of the study : Our study is among the very few RCTs that has compared the efficacy of LISA with InSurE using NIPPV as a primary mode of respiratory support, carried out in a large public hospital in LMIC. This study has large sample size with bigger and wider gestational age compared to other studies.

LIMITATION: This study has some limitations. As both the groups included different procedures; hence healthcare workers could not be blinded, but the study analysis was done by a statistician not involved in this research study. Our null hypothesis for primary outcome was true however the hypothesis for secondary outcome that LISA would be better in reducing rates of bpd in babies reqiring surfacatant administration was not true.This could be due to the fact that our study was not adequately powered for evaluating rates of bpd in babys recieving surfactant therapy.

CONCLUSION: To conclude, our study found LISA to be equally effective and safe compared to InSurE, as a method for surfactant administration in spontaneously breathing preterm neonates using NIPPV as a primary mode of respiratory support. We found insignificant statistical difference in the need for intubation within 72hours of birth between the two groups. The study is among very few trials comparing LISA with InSurE using NIPPV in preterms with a wide range of gestation between 28-36 weeks.

REFERENCES:

1. Wu X, Feng Z, Kong J, Lai Y, Jia C, Xu Z, et al. Efficacy and safety of surfactant administration via thin catheter in preterm infants with neonatal respiratory distress syndrome: A systematic review and meta-analysis. Pediatr Pulmonol. 2021 Sep;56(9):3013–25.

2. Halim A, Shirazi H, Riaz S, Gul SS, Ali W. Less Invasive Surfactant Administration in Preterm Infants with Respiratory Distress Syndrome. J Coll Physicians Surg–Pak JCPSP. 2019 Mar;29(3):226–330.

3. Polin RA, Carlo WA, Committee on Fetus and Newborn, American Academy of Pediatrics. Surfactant replacement therapy for preterm and term neonates with respiratory distress. Pediatrics. 2014 Jan;133(1):156–63.

4. Panza R, Laforgia N, Bellos I, Pandita A. Systematic review found that using thin catheters to deliver surfactant to preterm neonates was associated with reduced bronchopulmonary dysplasia and mechanical ventilation. Acta Paediatr Oslo Nor 1992. 2020 Nov;109(11):2219–25.

5. Blencowe H, Vos T, Lee AC, Philips R, Lozano R, Alvarado MR, et al. Estimates of neonatal morbidities and disabilities at regional and global levels for 2010: introduction, methods overview, and relevant findings from the Global Burden of Disease study. Pediatr Res. 2013 Dec;74(Suppl 1):4–16.

6. Dunn MS, Kaempf J, de Klerk A, de Klerk R, Reilly M, Howard D, et al. Randomized trial comparing 3 approaches to the initial respiratory management of preterm neonates. Pediatrics. 2011 Nov;128(5):e1069-1076.

7. Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, Lundstrom K, et al. Surfactant Therapy and Nasal Continuous Positive Airway Pressure for Newborns with Respiratory Distress Syndrome. N Engl J Med. 1994 Oct 20;331(16):1051–5.

8. Update of minimally invasive surfactant therapy [Internet]. [cited 2021 Nov 5]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5638833/

9. Pillow JJ, Minocchieri S. Innovation in surfactant therapy II: surfactant administration by aerosolization. Neonatology. 2012;101(4):337–44.

10. Attridge JT, Stewart C, Stukenborg GJ, Kattwinkel J. Administration of rescue surfactant by laryngeal mask airway: lessons from a pilot trial. Am J Perinatol. 2013 Mar;30(3):201–6.

11. Treatment of respiratory distress syndrome in premature infants: A comparison of LISA and INSURE methods in the Vietnamese context [Internet]. [cited 2021 Dec 16]. Available from: https://www.discoveryjournals.org/medicalscience/current_issue/v24/n104/A6.htm

12. Bhayat S, Kaur A, Premadeva I, Reynolds P, Gowda H. Survey of less Invasive Surfactant Administration in England, slow adoption and variable practice. Acta Paediatr Oslo Nor 1992. 2020 Mar;109(3):505–10.

13. Banerjee S, Fernandez R, Fox GF, Goss KCW, Mactier H, Reynolds P, et al. Surfactant replacement therapy for respiratory distress syndrome in preterm infants: United Kingdom national consensus. Pediatr Res. 2019 Jul;86(1):12–4.

14. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, te Pas A, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update. Neonatology. 2019;115(4):432–50.

15. Jay P Goldsmith, Edward H karotkin, Martin Keszler, Gautam K Suresh. Non Invasive Respiratory Support. In: Assisted Ventilation of the Neonate: An Evidence Bases ApproachTo Newborn Respiratory Care. 6th ed. Elsevier; p. 162–79.

16. Morley CJ, Davis PG, Doyle LW, Brion LP, Hascoet J-M, Carlin JB, et al. Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med. 2008 Feb 14;358(7):700–8.

17. Ramanathan R, Sekar KC, Rasmussen M, Bhatia J, Soll RF. Nasal intermittent positive pressure ventilation after surfactant treatment for respiratory distress syndrome in preterm infants <30 weeks' gestation: a randomized, controlled trial. J Perinatol Off J Calif Perinat Assoc. 2012 May;32(5):336–43.

18. Behnke J, Lemyre B, Czernik C, Zimmer K-P, Ehrhardt H, Waitz M. Non-Invasive Ventilation in Neonatology. Dtsch Ärztebl Int. 2019 Mar;116(11):177–83.

19. Lemyre B, Laughon M, Bose C, Davis PG. Early nasal intermittent positive pressure ventilation (NIPPV) versus early nasal continuous positive airway pressure (NCPAP) for preterm infants. Cochrane Database Syst Rev. 2016 Dec 15;12:CD005384.

20. Sai Sunil Kishore M, Dutta S, Kumar P. Early nasal intermittent positive pressure ventilation versus continuous positive airway pressure for respiratory distress syndrome. Acta Paediatr Oslo Nor 1992. 2009

Sep;98(9):1412–5.

21. Shi Y, Tang S, Zhao J, Shen J. A prospective, randomized, controlled study of NIPPV versus nCPAP in preterm and term infants with respiratory distress syndrome. Pediatr Pulmonol. 2014 Jul;49(7):673–8.

22. Jena SR, Bains HS, Pandita A, Verma A, Gupta V, Kallem VR, et al. Surfactant therapy in premature babies: SurE or InSurE. Pediatr Pulmonol. 2019 Nov;54(11):1747–52.

23. Jensen EA, Dysart K, Gantz MG, McDonald S, Bamat NA, Keszler M, et al. The Diagnosis of Bronchopulmonary Dysplasia in Very Preterm Infants. An Evidence-based Approach. Am J Respir Crit Care Med. 2019 Sep 15;200(6):751–9.

24. Verder H, Agertoft L, Albertsen P, Christensen NC, Curstedt T, Ebbesen F, et al. [Surfactant treatment of newborn infants with respiratory distress syndrome primarily treated with nasal continuous positive air pressure. A pilot study]. Ugeskr Laeger. 1992 Jul 27;154(31):2136–9.

25. Kattwinkel J, Robinson M, Bloom BT, Delmore P, Ferguson JE. Technique for intrapartum administration of surfactant without requirement for an endotracheal tube. J Perinatol Off J Calif Perinat Assoc. 2004 Jun;24(6):360–5.

26. Herting E, Härtel C, Göpel W. Less invasive surfactant administration: best practices and unanswered questions. Curr Opin Pediatr. 2020 Apr;32(2):228–34.

27. Bao Y, Zhang G, Wu M, Ma L, Zhu J. A pilot study of less invasive surfactant administration in very preterm infants in a Chinese tertiary center. BMC Pediatr. 2015 Mar 14;15:21.

28. Mohammadizadeh M, Ardestani AG, Sadeghnia AR. Early administration of surfactant via a thin intratracheal catheter in preterm infants with respiratory distress syndrome: Feasibility and outcome. J Res Pharm Pract. 2015 Mar;4(1):31–6.

29. Gupta BK, Saha AK, Mukherjee S, Saha B. 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. Eur J Pediatr. 2020 Aug;179(8):1287–93.

30. Akçay N, Gökalp A, Gunlemez A, Oğuz D, Kılıçbay F, Arısoy A. Comparison of LISA vs INSURE Technique Using Nasal Intermittent Positive Pressure Ventilation (NIPPV) Support In Preterm Infants: A Randomized Controlled Trial Preterm Bebeklerde Nazal Aralıklı Pozitif Basınçlı Ventilasyon (NIPPV) Desteği kullanılarak LISA ile INSURE Tekniğinin Karşılaştırılması: Randomize Kontrollü Bir Çalışma-NonCommercial 4.0 International (CC BY). Bakirkoy Tip Derg Med J Bakirkoy. 2021 Mar 31;1–6.

31. Buyuktiryaki M, Alarcon-Martinez T, Simsek GK, Canpolat FE, Tayman C, Oguz SS, et al. Five-year single center experience on surfactant treatment in preterm infants with respiratory distress syndrome: LISA vs INSURE. Early Hum Dev. 2019 Aug;135:32–6.

32. Silahli M, Tekin M. The Comparison of LISA and INSURE techniques in term of neonatal morbidities and mortality among premature infants. Acta Bio-Medica Atenei Parm. 2020 Nov 10;91(4):e2020189.

33. Yang S, Kim Y, Lee B. Comparison Between Less Invasive Surfactant Administration (LISA) and Intubation-Surfactant-Extubation (InSurE) in Preterm Infants with Respiratory Distress Syndrome: A Retrospective Study. 2020.

34. Pareek P, Deshpande S, Suryawanshi P, Sah LK, Chetan C, Maheshwari R, et al. Less Invasive Surfactant Administration (LISA) vs. Intubation Surfactant Extubation (InSurE) in Preterm Infants with Respiratory Distress Syndrome: A Pilot Randomized Controlled Trial. J Trop Pediatr. 2021 Aug 27;67(4):fmab086.

35. Göpel W, Kribs A, Ziegler A, Laux R, Hoehn T, Wieg C, et al. Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): an open-label, randomised, controlled trial. Lancet Lond Engl. 2011 Nov 5;378(9803):1627–34.

36. Kanmaz HG, Erdeve O, Canpolat FE, Mutlu B, Dilmen U. Surfactant administration via thin catheter during spontaneous breathing: randomized controlled trial. Pediatrics. 2013 Feb;131(2):e502-509.

37. 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):F17–23.

38. Isayama T, Iwami H, McDonald S, Beyene J. Association of Noninvasive Ventilation Strategies With Mortality and Bronchopulmonary Dysplasia Among Preterm Infants: A Systematic Review and Meta-analysis. JAMA. 2016 Aug 9;316(6):611–24.

39. Jourdain G, De Tersant M, Dell'Orto V, Conti G, De Luca D. Continuous positive airway pressure delivery during less invasive surfactant administration: a physiologic study. J Perinatol Off J Calif Perinat Assoc. 2018 Mar;38(3):271–7.

40. Aghai ZH, Saslow JG, Nakhla T, Milcarek B, Hart J, Lawrysh-Plunkett R, et al. Synchronized nasal intermittent positive pressure ventilation (SNIPPV) decreases work of breathing (WOB) in premature infants with respiratory distress syndrome (RDS) compared to nasal continuous positive airway pressure (NCPAP). Pediatr Pulmonol. 2006 Sep;41(9):875–81.

41. Efficacy of noninvasive respiratory support modes for primary respiratory support in preterm neonates with respiratory distress syndrome: Systematic review and network meta-analysis - PubMed [Internet]. [cited 2021 Dec 22]. Available from: https://pubmed.ncbi.nlm.nih.gov/32762014/

42. Li W, Long C, Zhangxue H, Jinning Z, Shifang T, Juan M, et al. Nasal intermittent positive pressure ventilation versus nasal continuous positive airway pressure for preterm infants with respiratory distress syndrome: a meta-analysis and up-date. Pediatr Pulmonol. 2015 Apr;50(4):402–9.

43. Kiciman NM, Andréasson B, Bernstein G, Mannino FL, Rich W, Henderson C, et al. Thoracoabdominal motion in newborns during ventilation delivered by endotracheal tube or nasal prongs. Pediatr Pulmonol. 1998 Mar;25(3):175–81.

44. Queliz T, Perez JA, Corrigan MJ. A comparison of LISA versus InSurE: A single center experience. J Neonatal-Perinat Med. 2021;14(4):503–9.

45. Oncel MY, Arayici S, Uras N, Alyamac-Dizdar E, Sari FN, Karahan S, et al. Nasal continuous positive airway pressure versus nasal intermittent positive-pressure ventilation within the minimally invasive surfactant therapy approach in preterm infants: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed. 2016 Jul;101(4):F323-328.

46. Olivier F, Nadeau S, Bélanger S, Julien A-S, Massé E, Ali N, et al. Efficacy of minimally invasive surfactant therapy in moderate and late preterm infants: A multicentre randomized control trial. Paediatr Child Health. 2017 Jun;22(3):120–4.

47. Bellos I, Fitrou G, Panza R, Pandita A. Comparative efficacy of methods for surfactant administration: a network meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2021 Sep;106(5):474–87.