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Original Research Article

RANDOMIZED CONTROLLED TRIAL OF LISA V/S INSURE TECHNIQUE OF SURFACTANT ADMINISTRATION IN PRETERM NEONATES WITH RDS BETWEEN 28-34 WEEKS OF GESTATION

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ABSTRACT

Background: To compare LISA vs InSurE technique of surfactant administration on need for mechanical ventilation in Preterm Neonates with RDS between 28-34 weeks of Gestation.

Materials and Methods: Randomised controlled trial done in preterm neonates of 28-34 weeks of Gestation with RDS, admitted in SNCU Inborn at Niloufer hospital for a period of 2 years. Preterm neonates of 28-34 weeks of gestation, Clinical Diagnosis of RDS with persistent fi02 requirement >30% in first 6 hrs of life are included in study. we compared the requirement of 2nd dose of surfactant, incidence of BPD and complications of Prematurity in both the groups.

Results: The most common cause of prematurity in LISA and INSURE groups is PPROM, followed by Fetal distress. Least common cause of prematurity in LISA and INSURE groups are Antepartum haemorrhage and Twin delivery-PROM respectively. The median of time from birth to the onset of procedure in both LISA group and INSURE group is similar and is 4 hours. The mean Fio2 at the beginning of the procedure among the LISA group, mean Fio2 at the 1st hour after the procedure, mean Fio2 at the 4th hour after procedure are insignificant. None of the adverse effects are significant when compared in groups. Median period in days of NIV, Repeat dose of surfactant, median length of hospital stay and Bradycardia is insignificant. Desaturation was not significant. The median duration of supplemental O2 in LISA group was 5 days, whereas in INSURE group was 8 days. The difference is statistically significant with $p < 0.05$. 55 patients (68.75%) in the LISA group and in 59 patients (73.75%) in the INSURE group survived which is not statistically significant.

Conclusions: Although the research suggests that LISA is superior in terms of outcome, our study demonstrated that LISA is superior in terms of minimising the period of oxygen supplementation and hospital stay. However, we found no substantial difference in other outcomes.

Keywords: Respiratory Distress Syndrome (RDS), less invasive surfactant administration (LISA), Intubation-Surfactant Extubation (InSurE).

INTRODUCTION

The intubation, surfactant, and extubation procedure (InSurE), which entails tracheal intubation, surfactant administration, and extubation, has traditionally been used to administer surfactant to preterm infants with respiratory distress syndrome (RDS) who need surfactant therapy. However, less intrusive techniques, such as minimally invasive or less invasive surfactant therapy, have lately been found to be effective. These techniques decrease airway damage and barotrauma by avoiding intubation. This randomised trial's main goal is to assess how often mechanical ventilation (MV) was

necessary when using either the InSurE approach or administering surfactant through a thin catheter while the patient was spontaneously breathing.[1,2]

In the recent times there has been a number of studies all over the world suggesting LISA has better outcome than InSurE but those results cannot be Extrapolated to low socio-economic countries like India, due to unavailability and affordability issues of Surf catheters which are being used in developed countries for LISA technique. In India, few studies have been conducted with alternative and cheaper methods by using Feeding tube instead of SurfCath for Administration of Surfactant in LISA technique out of which only one study showed LISA has better outcome than InSurE technique. Hence, we need to conduct more studies to come to the conclusion that LISA is better than InSurE technique in low socio-economic countries like India.

MATERIALS AND METHODS

Randomised controlled trial done in preterm neonates of 28-34 weeks of Gestation with RDS, admitted in SNCU Inborn at Niloufer hospital for a period of 2 years.

Inclusion Criteria

1. Preterm of 28-34 weeks of gestation
2. Clinical Diagnosis of RDS with persistent fi02 requirement >30% in first 6 hrs of life.
3. Informed consent of the parent.

Exclusion Criteria

1. Babies who were intubated for any reason.
2. Major Congenital malformations requiring surgical correction ex: maxillo-facial, tracheal, or known pulmonary malformations, complex congenital heart disease.
3. Alternative cause for respiratory distress e.g: congenital pneumonia, MAS, severe lung atelectasis.
4. Intraventricular hemorrhage (> grade 2)

Sample Size: 160 (80 in each group)

Based on the previous study Conducted by Venkat R. Kallem, Soumya R. Jena MD[3] in india The incidence of need for Mechanical ventilation in the LISA group is found to be 19% & INSURE group is 40%. With the Power of study with 80%, Alpha error of 0.05 my sample size was around 146, considering the 10% as Dropout, my Total Sample size is 160 (80 in each group). Preterm neonates born between 28-34 weeks who developed RDS within 6hrs of life were put on Continuous Positive Pressure Ventilation (CPAP). Babies who required a fraction of inspired oxygen (Fi02) more than 30% on CPAP of 6 cm H20 to maintain saturation between 90%and 95% in the first 6 hours of life were randomized to receive surfactant either by LISA or InSurE technique. Randomization was done by computer- generated random sequence numbers for which Gigacalculator.com was used for generating random sequence numbers from 1 - 160. Allocation ratio was 1:1 for LISA and InSurE respectively and concealment was done by using an opaque sealed envelope. The need for MV within the first 72 hours and other related outcomes will be analyzed between the two groups.

InSurE Procedure: Intubate-Surfactant-Extubate (InSurE)

Neonates who were fulfilled with the criteria for surfactant administration after trail of CPAP were given by InSurE technique. Before the procedure, 5Fr Feeding tube length was measured till the length of appropriate size ET tube and was cut 1 cm distal to the end under aseptic conditions. Endotracheal intubation with Appropriate size ET tube was done and secured at an appropriate length and connected to Mechanical ventilator. The surfactant was filled in a 10cc syringe and slowly instilled into the airway through a Feeding tube of 5Fr inserted into Endotracheal tube over 60 sec, followed by pushing 3 ml of Air. If there was hypoxia or bradycardia the rate of surfactant administration was reduced. FiO2 was titrated to keep oxygen saturation between 90 and 95% (Despite this if there was persistent apnea / Bradycardia Terminate the procedure and PPV was given). Then the baby was extubated to non-invasive NCPAP (nasal continuous positive airway pressure)-assisted breathing within 30-60mins.

LISA: Less Invasive Surfactant Administration

The neonates who had been allocated for LISA technique, before the procedure Feeding tube 7Fr size was used and the required depth was calculated (from the Proximal end of the tube) as Nasal-tragus length plus Icm & feeding tube was cut at the distal end.

Another Feeding tube was placed into the stomach and aspirated the fluid present in the stomach, which helps to deflate the stomach and increase lung expansion. Neonates will be spontaneously breathing with nasal CPAP support under multi-channel monitoring

Surfactant was brought to a room temperature, and drawn in a 10cc syringe. Before starting the Procedure made sure the baby was Stable & was connected to the Monitor (Note the Vitals & CPAP Settings). With the Help of Laryngoscope, glottis was visualized and the OG tube was inserted through the glottis.

Once the OG tube was seen passing through the cords the laryngoscope was withdrawn while ensuring the OG tube remained in-situ, taking note of the marking on the catheter which is at the lips and the head returned to a neutral position.

The Surfactant syringe is then attached to the OG tube & surfactant is slowly injected into the catheter over 60-90 sec to minimize apnea / bradycardia. If there was hypoxia or bradycardia the rate of surfactant administration was reduced. FiO2 was titrated to keep oxygen saturation between 90 and 95%. (Despite this if there was persistent apnea / Bradycardia, procedure is stopped for 1-2 mins and PPV was given if required)

After pushing the surfactant , then 3 ml of Air was pushed into the feeding tube to clear any remnants of surfactant within the tube. Feeding tube was removed and the baby was continued on CPAP. Feeding tube

which was inserted in to the stomach is aspirated to confirm no Surfactant was instilled in the stomach. If there is difficulty in performing the procedure, then it was considered as failure of LISA technique , then InSurE Technique was performed.

Statistical Analysis: The data analysis was done on Epi info 7. Variables of interest was expressed in percentages, means (standard deviation) for normally distributed continuous variables, and median (range) for variables not normally distributed. Mann-Whitney U test and chi square test was used to compare baseline differences between the infants in the LISA and InSurE groups.

RESULTS

The number of males in LISA group are 46 (57.5%), number of females in LISA group are 34 (42.5%). The number of males in INSURE are 38 (47.5%) and the number of females in INSURE are 42 (52.5%).

Table 1: ?

Gender	**LISA**	**INSURE**
Male	46 (57.5%)	38 (47.5%)
Female	34 (42.5%)	42 (52.5%)
Birth weight		
Mean	1300.12+/- 274.01	1280.87 +/- 267.44
ELBW	10 (12.5%)	10 (12.5%)
VLBW	46 (57.5%)	49 (61.25%)
LBW	24 (30%)	21 (26.25%)
Antenatal steroids		
Yes	60	64
No	20	16
Gestational age		
Mean	30.63 +/- 1.96	30.7 +/- 1.90
28-31 weeks	55	53
32-33 weeks	16	20
>33 weeks	9	7

All demographic details are comparable in present study

Table 2: Pre-natal complications leading to premature birth

Complication	**LISA**	**%**	**INSURE**	**%**
Antepartum hemorrhage	4	5	4	5
Bleeding PV	6	7.5	5	6.25
Doppler changes	5	6.25	5	6.25
Fetal distress	18	22.5	22	27.5
PPROM	30	37.5	28	35
Pre Eclampsia	10	12.5	13	16.25
Twin delivery, PROM	7	8.75	3	3.75

The most common cause of prematurity in LISA and INSURE groups is PPROM, followed by Fetal distress. Least common cause of prematurity in LISA and INSURE groups are Antepartum haemorrhage and Twin delivery-PROM respectively.

Table 3: Time from birth to procedure

Median of the time from birth to procedure in hours	**LISA**	**INSURE**
Time in hours	4 (3 - 5)	4(3-5)
Mean FiO2 at the beginning of the procedure	44% (30% - 50%)	41% (30% - 50%)
Mean FiO2 at 1st hour after the procedure	44% (30% - 70%)	42% (30% - 70%)
Mean FiO2 at 4th hour after the procedure	39% (21% - 100%)	39% (30% - 100%)

The median of time from birth to the onset of procedure in both LISA group and INSURE group is similar and is 4 hours. The mean Fio2 at the beginning of the procedure among the LISA group was 44% and the Mean Fio2 at the beginning of the procedure among the INSURE group was 41%. The difference is not statistically significant at p=0.062. The mean Fio2 at the 1st hour after the procedure among the LISA group was 44% and the Mean Fio2 at 1st hour after the procedure among INSURE group was 42%. The difference is not statistically significant at $p < 0.05$ (0.242). The mean Fio2 at the 4th hour after the procedure among the LISA group was 39% and the Mean Fio2 at 4th hour after the procedure among INSURE group was 39%.

Table 4: Mechanical ventilation within 72 hrs of life

Variable	LISA	INSURE	*P* value
Mechanical ventilation within 72 hours of birth	16	20	>0.05

Relative risk = 0.8, Odds ratio = 0.75

16 patients (20%) from the LISA group were intubated within 72 hours of birth in LISA group, whereas 20 patients (25%) from INSURE group were intubated within 72 hours of birth. The difference is not statistically significant with p value > 0.05.

Table 5: Adverse effects in patients of study

Intraventricular Hemorrhage	LISA	INSURE
Yes	8	11
No	72	69
Hemodynamically significant patent ductus arteriosus		
Yes	10	12
No	70	68
Necrotising Enterocolitis		
Yes	8	7
No	72	73
Bronchopulmonary Dysplasia		
Yes	2	5
No	55	54
Pneumothorax		
Yes	1	2
No	79	78
Periventricular Leukomalacia		
Yes	6	8
No	49	51

None of the adverse effects are significant when compared in groups.

Table 6: Duration on NIV in days

Time period of NIV in days	LISA	INSURE
Median days (IQR)	3(2-5)	3.5 (3 - 5)
Repeat dose of surfactant		
Yes	11	13
No	69	67
Median days (IQR)	10 (8 - 19)	14 (10 - 17)
Adverse events		
Yes	12	17
No	68	63
Reflux of surfactant		
Yes	12	10
No	68	70

The median period in days of NIV for patients from LISA group was 3 days and for INSURE group was 3.5 days. The difference is not significant (Mann-Whitney U test) with p value >0.05 (0.21). Repeat dose of surfactant was required in 11 patients (13.75%) in the LISA group and in 13 patients (16.25%) in the INSURE group. The difference is not statistically different at p value > 0.05. Chi-square = 0.19, P value= 0.65

The median length of hospital stay for patients from LISA group was 10 days and for INSURE group was 14 days. The difference is statistically significant (Mann-Whitney U test) with p value <0.05 (0.007) Bradycardia during surfactant administration was noted in 12 patients (15%) in the LISA group and in 17 patients (21.25%) in the INSURE group. The difference is not statistically different at p value > 0.05. Chi-square = 0.97. Reflux of surfactant was noted in 12 patients (15%) in the LISA group and in 10 patients (12.5%) in the INSURE group. The difference is not statistically different at p value > 0.05. Chi-square = 0.21.

Table 7: Desaturation <80% and median duration of supplemental O2

Desaturation <80%	LISA	INSURE
Yes	13	19
No	67	61
Median duration of supplemental O2		
Median days (IQR)	5(2-6)	8(4-9)

Desaturation was noted in 13 patients (16.25%) in the LISA group and in 19 patients (23.75%) in the INSURE group. The difference is not statistically different at p value > 0.05. Chi-square = 1.40 The median duration of

supplemental O2 in LISA group was 5 days, whereas in INSURE group was 8 days. The difference is statistically significant with $p < 0.05$.

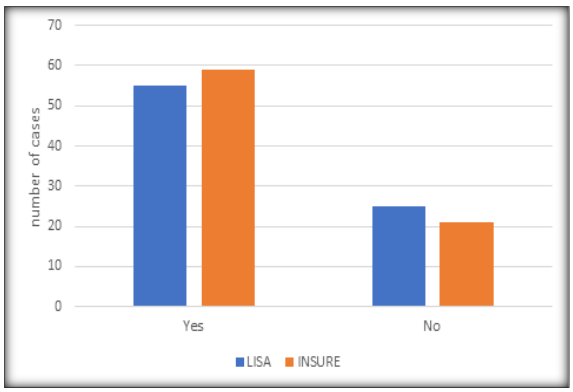

Figure 1: Survival of patients in the group

55 patients (68.75%) in the LISA group and in 59 patients (73.75%) in the INSURE group survived. The difference is not statistically different at p value > 0.05. Chi-square = 0.48.

DISCUSSION

The baseline characteristics in both the groups were comparable which included Gender, gestational age, Birth weight, antenatal steroids, Cause of prematurity, median of time from birth to procedure, Mean FiO2 at the start of procedure, at 1st hour and at 4th hour. Similar to our study, a number of previous studies reported no discernible difference between the InSurE and LISA group in terms of the requirement for intubation and MV within 72 hours of birth. In a single centre, randomized controlled trial (RCT) involving 90 spontaneously breathing preterm children between the ages of 28 and 32 weeks, Bao et al,[4] observed no significant changes in the rate of MV in the first 72 hours. Similar results were observed in an Iranian multicenter RCT Conducted by Mohammadizadeh et al.[5] In which preterm infants ≤34 weeks' gestation and weighing 1,000–1,800 g on CPAP and FiO2 ≥0.30 or moderate work of breathing within the first hour of life were randomized to receive 200 mg/kg poractant alfa by either a 6-Fr feeding tube or by the InSurE technique. Study Conducted by Urszula Kaniewska et al.[6] Poland and Mohammad Kazem Sabzehei et al.[7] Iran 2022 also did not any difference between LISA and InSurE groups in terms of MV within 72 hrs of life. There are very few Indian studies comparing LISA vs InSurE, among them the following 3 studies did not show any difference between LISA and InSurE groups in terms of mechanical ventilation within 72 hrs of birth. Bhupendra Kumar Gupta et al,[8] India a total of 58 infants with gestational age of 28-34 weeks were randomized to one of the two groups ofLISA and InSurE, there was no statistically significant difference in need of IMV in 72 h of life between the two groups. Prince Pareek MD, et al,[9] in this total of 40 infants with gestational age between 28 - 36 weeks were randomized into two groups, and study concluded there was no statistically significant difference between the two groups in terms of MV within 72 hrs of life. Aradhana Mishra et al.[10] A total of 150 neonates were randomized to one of the two groups of LISA and InSurE There was statistically insignificant difference in the need for intubation within 72 h of birth between the InSurE and LISA group. There was less need for invasive ventilation in the LISA group when compared to the intubation group, according to numerous other trials conducted in various parts of the world and meta-analyses.

Vincent Rigo et al11 review and meta-analysis included 6 RCTs which investigated respiratory outcomes for preterm infants with respiratory distress syndrome treated with LISA rather than administration of surfactant through an endotracheal tube (INSURE). LIST resulted in decreased invasive ventilation requirements. A multicentre randomized control trial39 François Olivier et al,[12] Canada This study included 3 Canadian Centres with 45 patients, 24 in LISA group and 21 in INSURE group concluded significant reduction of MV exposure in LISA group. A systematic review and meta-analysis. Jose C Aldana-Aguirre et al13 six RCTs were included in this Trial, the results included the use of LISA technique reduced the need for mechanical ventilation within 72 hours of birth or need for mechanical ventilation anytime during the neonatal intensive care unit stay. Five-year single center experience conducted by Mehmet Buyuktiryaki et al,[14] This retrospective cohort study included 205 LISA-treated and 178 INSURE-treated infants revealed The mechanical ventilation requirement in the first 72h of life were lower in LISA-treated infants. A recent study conducted by Hyung-Joon Joo et al,[15] concluded that the LISA group had lower rates of mechanical ventilation (MV) 72 hours after birth and at any time. Systematic review conducted by Raffaella Panza, Aakash Pandita,[16] used PubMed, Embase, Cochrane Library and Web of Science databases identified papers published up to 5th November 2019. It included 15 studies covering 4,926 preterm infants, including 6 RCTs, 7 observational studies and 2 feasibility studies, showed significant reductions in early intubation rates with less invasive surfactant administration (LISA). Among the Indian studies, only one study conducted by Soumya R. Jena MD et al,[17] which included a total of 350 babies with gestational age <34 weeks were randomized to one of the two groups, Results concluded there was a significant reduction in the need for MV in the LISA group. Instead of using pressure limited volume guarantee breathing by T-piece, InSurE was performed in our study using Self inflated AMBU. This could create a bias for potential lung damage. Median duration of Surfactant Administration from birth to procedure in Sowmya R. Jena is 1 hr but in our study it was 4 hours. In there study they have used Neosurf as a

single surfactant, but in our study the surfactant used was Beractant and Curosurf depending upon the availability. This factors might have interfered with the results in our study.

In our study it was found that repeat dose of surfactant was required more in InSurE group when compared to LISA group but this was statistically not significant. Similar to our study, In study conducted by Mohammad Kazem Sabzehei et al,[7] it was observed that repeat dose of surfactant was needed less in the LISA group but this was statistically insignificant. Other studies conducted by Jose C Aldana-Aguirre et al,[13] Soumya R. Jena MD et al,[17] Bhupendra Kumar Gupta et al,[8] Aradhana Mishra et al,[10] showed that there was no difference in doses required between the two groups. However in the study conducted by Mohamed I. Garib et al.18 Second dose of Surfactant administration requirement was more in MIST group compared to the INSURE group and was statistically significant.

In our study it is found that the median duration of supplemental O2 among survivors in the LISA group was 5 days, whereas in the INSURE group was 8 days. The difference is statistically significant with $p < 0.05$. Our results were similar with the results obtained in study conducted by Soumya R. Jena MD et al.[17] This can be explained on the basis of animal studies which have shown a few mechanical breaths are sufficient to cause lung injury in the neonatal period. Other studies did not show significant difference between the two groups.

In our study the median length of hospital stay for patients from the LISA group was 10 days and for INSURE group was 14 days. The difference is statistically significant (Mann-Whitney U test) with p value <0.05 (0.007). Similar results were seen in studies Soumya R. Jena MD et al,[17] Mohammadizadeh et al, and Mohammad Kazem Sabzehei et al,[7] which showed that the length of hospital stay was significantly less in LISA group when compared to InSurE group. Studies conducted by Mehmet Buyuktiryaki et al,[14] Prince Pareek MD et.al,[9] 2021 and Aradhana Mishra et al,[10] didn't show significant difference between the two groups. Numerous other factors have a big impact on it, including complications that arise during NICU stays (sepsis, growth and feeding issues), social factors (parental presence and efficacy), and public health considerations (availability of beds, existence of back transfer protocols, second level hospital, etc.)

The median period in days of NIV requirement for patients from LISA group was less (3 days) when compared to InSurE group (3.5 days), but the difference was not statistically significant. Similar to our study, studies conducted by Urszula Kaniewska et al,[2] Bhupendra Kumar Gupta et al,[8] Prince Pareek MD et.al,[9] also did not show any significant difference between LISA and InSurE groups. Studies conducted by Vincent Rigo et al,[11] and Hyung-Joon Joo et al,[15] showed that duration of NIV requirement was significantly less in LISA group when compared to InSurE group. However studies conducted by Musa Silahli et al. and Mohamed I. Garib et al,[18] showed that duration of NIV requirement for the LISA group was significantly higher when compared to LISA group , which was against our results. Musa attributed it to the use of different nasal prongs in our study.

In our study it was found that there was no significant difference between LISA and InSurE groups with respect to development of Intraventricular Hemorrhage (Ivh). Similar results were seen in studies conducted by Jose C Aldana-Aguirre et al.[13] Soumya R. Jena MD et al,[17] Mehmet Buyuktiryaki et al,[14] Urszula Kaniewska et al.[2] In A Systematic Review and Meta-Analysis , conducted by Lirong Wang et al,[19] which included 21 research articles were eligible, comprising 19,976 study participants, it showed Development of IVH was less in LISA group but was statistically significant. But in Study conducted by Prince Pareek MD, et.al,[9] it was found that IVH was more in LISA group than InSurE group but it was not statistically significant.

2 patients from the surviving babies in the LISA group (3.5%) had BPD as a complication and 5 patients (8.62%) from surviving babies in the INSURE group had Bronchopulmonary Dysplasia as a complication and the difference is not statistically significant at $p > 0.05$. (Chi-square =1.26). Similar to our study, Six studies reported on BPD, defined as oxygen requirement at 36 weeks' postmenstrual age. Bao et al4 and other studies none of this trials individually reported a decrease in BPD with LISA group. Recently conducted trail by Urszula Kaniewska et al,[2] also did not Significant difference between the two groups. But studies conducted by Mehmet Buyuktiryaki et al,[14] Vincent Rigo et al,[11] Jose C Aldana-Aguirre et al,[13] Raffaella Panza,[16] Aakash Pandita,[16] Lirong Wang et al.[19] (Systemic Review) showed there is significant decrease in BPD in LISA group when compared to InSurE group.

There was no significant difference between the two groups with respect to Desaturation and bradycardia during the procedure. Similar results were seen with the study conducted by Prince Pareek MD, et.al.[9] But the studies conducted by Hyung-Joon Joo et al. 2022 Korea51 and Mohammad Kazem Sabzehei et al,[7] showed that adverse effects were less in LISA group when compared to InSurE group.

In our study 1 case developed Pneumothorax in LISA group and 2 cases in InSurE group and this difference was not statistically significant. Many studies did not show any significant difference between the two groups except for studies conducted by Oliver et al,[12] Lirong Wang et al.[19] (Systemic Review) which showed there was a significant decrease in incidence of Pneumothorax in LISA group when compared to InSurE group.

In our study it was found that there was no significant difference between LISA and InSurE groups with respect to development of hemodynamically significant patent ductis arteriosus. Similar results were seen in studies conducted by Jose C Aldana-Aguirre et al,[13] Soumya R. Jena MD et al,[17]

Mehmet Buyuktiryaki et al,[14] Urszula Kaniewska et al2. In A Systematic Review and Meta-Analysis, conducted by Lirong Wang et al,[19] which included 21 research articles were eligible, comprising,[19] 976 study participants, it showed Development of IVH was less in LISA group but was statistically significant. But in Study conducted by Prince Pareek MD, et.al,[9] and Mohammad Kazem Sabzehei et al,[7] found that HsPDA was more in LISA group than InSurE group but it was not statistically significant.

In our study it was found that there was no significant difference between LISA and InSurE groups with respect to development of Necrotising Enterocolitis. Similar results were seen in studies conducted by Jose C Aldana-Aguirre et al,[13] Soumya R. Jena MD et al,[17] Mehmet Buyuktiryaki et al,[14] Urszula Kaniewska et al.[2] In Systemic Review conducted by Lirong Wang et al.[19] China 2022, which included,[21] research articles were eligible, comprising,[19] 976 study participants, it showed Development of NEC was less in LISA group and was statistically significant. Recent Indian study conducted by Soumya R. Jena MD et al44 also showed significant reduction in NEC in LISA group.

Our study did not show significant difference between the two groups in terms of PVL as a complication, which is similar with most of the studies.

In our study it was found that the death rate was more in the LISA group (n=25, 31.25%) in comparison with the InSurE group (n=21, 26.25%) but this difference was not statistically significant. In both the groups sepsis was the common cause of death. Although the research suggests that LISA is superior in terms of outcome, our study demonstrated that LISA is superior in terms of minimising the period of oxygen supplementation and hospital stay. However, we found no substantial difference in other outcomes. This could be owing to the diversity of paediatricians' procedures, and there was no uniformity in prenatal steroids, which we know have a significant role in the prevention of RDS in preterm newborns by stimulating type 2 pneumocytes to produce Surfactant. Sepsis was shown to be the leading cause of mortality in both groups, which may have had an indirect influence in the need for mechanical ventilation and associated issues. Finally, in both groups, we did not utilise premedication before to the procedure to avoid respiratory depression. Pain has the potential to have both short- and long-term neurological consequences on the developing brain. The dangers of not taking premedication must be balanced against the hazards of sedation during LISA.

Limitations

Uniformity in Antenatal steroids: As antenatal steroids play a major role in prevention of RDS, this factor should have been taken in inclusion criteria which was not done in our study.

Equally Trained neonatologist: Equally Trained pediatricians should be performing the procedures as this may avoid difference in technique of procedure and may reduce differences between the outcomes in the same group.

Surfactant: The surfactant used was Beractant or Curosurf based on the availability, hence there should be uniformity in the usage of Surfactant.

Sepsis: As we know sepsis plays an important role in neonatal mortality and morbidity hence strict aseptic precautions have to be taken, which reduces the sepsis related deaths and even reduces the complications.

NIPPV vs CPAP: As we have used CPAP as a primary mode of NIV, but literature says NIPPV is better than CPAP in prevention of Mechanical ventilation, hence attempt has to be made to use NIPPV as primary mode of NIV

CONCLUSION

We found LISA to be equally effective as InSurE for surfactant administration in the treatment of RDS in preterm infants. However LISA may decrease the duration of supplemental oxygen requirement and also length of hospitalization. Future larger RCTs are required to compare the efficacy and long-term outcomes of LISA with the standard invasive methods of surfactant administration.

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