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Original Article

Less Invasive Surfactant Administration (LISA) in Premature Neonates, using 5F feeding tube versus 2 mm Endotracheal tube – An Innovative, Pilot study

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Abstract

Introduction: Administration of LISA using thin and soft catheters like 5 F orogastric tube, though less invasive, is technically challenging and needs expertise. We hypothesized, use of a 2 mm Endotracheal (ET) tube for administration of LISA could be an easy and convenient alternative.

Methods: This is a prospective, single-centric, quasi-random, pilot trial conducted in the inborn unit of a tertiary care hospital from May 2020 - December 2020. All the inborn preterm (28 - 34 weeks) neonates with respiratory distress requiring surfactant were alternately allocated to receive LISA using a 5 F infant feeding tube or an uncuffed 2.0 size ET tube. The primary outcome was successful administration of surfactant defined as a procedure without any need for positive pressure ventilation.

Results: In our study, 25 neonates were enrolled in each arm. Administration of LISA using 2 mm ET tube was associated with better success of surfactant administration with lesser incidence of PPV (20 vs 11, $p < 0.05$), desaturation (5 vs 12, $p < 0.05$), and bradycardia (3 vs 10, $p < 0.05$) compared to LISA-OG.

Conclusions: Administration of LISA using a 2 mm ET is an easily adaptable and convenient alternative that is well tolerated by the neonates without any adverse effects.

Introduction

Early initiation of continuous positive airway pressure (CPAP), right from the labour room, prevents alveolar collapse and atelectasis. Nasal CPAP (nCPAP) is a non-invasive and currently recommended initial support strategy for preterm neonates with respiratory distress syndrome (RDS).[1] Worsening of RDS needs an escalation of support, which includes timely surfactant administration.[2] Less invasive surfactant administration (LISA) technique is a gentle approach of surfactant administration and includes the administration of surfactant to a spontaneously breathing neonate while continuing nCPAP throughout the procedure. Numerous trials and recent meta-analyses indicate that the LISA technique helps to reduce the duration of mechanical ventilation and is also associated with numerous improved outcomes like prevention of bronchopulmonary dysplasia (BPD) and intracranial hemorrhage (ICH).[3-6]

LISA can be administered by using four techniques: using a thin catheter, laryngeal mask airway, pharyngeal surfactant delivery, and aerosolized surfactant therapy. While aerosolized surfactant delivery remains truly non-invasive, thin catheter administration (TCA) is the most popular and practical technique. By now, a variety of different LISA catheters (Gastric tubes, suction catheters, umbilical catheters, bladder catheters and various commercial semi-rigid catheters developed for LISA like Lisacath, surfcath), devices and techniques have been described, however there lacks standardization regarding the techniques across various units and countries.[7]

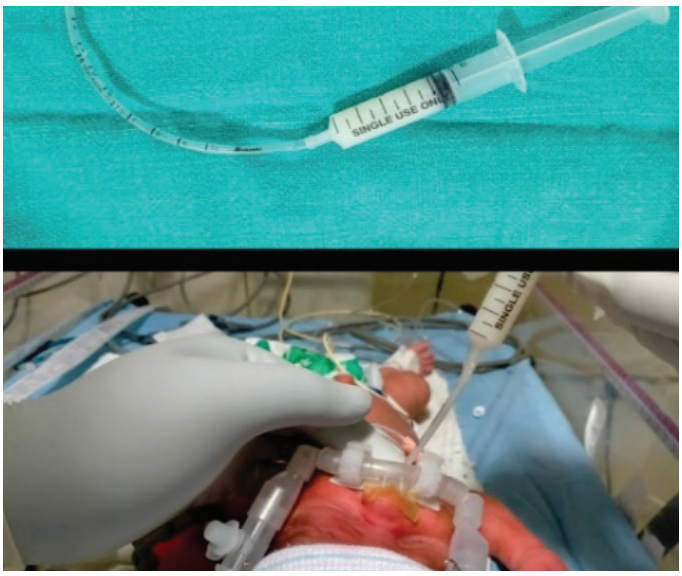
LISA using an infant feeding tube can be practiced with or without using Magill forceps and remains technically more difficult to master than conventional intubation. It was found to be associated with the following adverse effects in literature – need for more than one attempt (in 5 to 30%), apnea requiring positive pressure ventilation (PPV) n (12 - 44%), significant bradycardia or desaturation (10 - 30%), dislocation of the catheter (1%), surfactant reflux (3-40%).[8] LISA using semirigid catheters like the LISA catheter, is easier to practice, however, their availability, cost factor, and logistic issues are the limitations for their routine use.[9,10]

To retain the benefits and avoid the above-mentioned adverse events, we innovated the use of a familiar and well-versed rigid catheter - the smallest endotracheal (ET) tube available, the 2.0 mm one whose diameter is equivalent to the infant feeding tube of size 8 F for the administration of LISA.

Methods

This is a prospective, single-centric, quasi-random, pilot trial conducted in the inborn unit of a tertiary care hospital at Hyderabad, India from May 2020 to December 2020. The study was approved by the institutional ethical committee and written informed consent by the parents was obtained. Inborn neonates between 28 to 34 weeks of gestational age, with respiratory distress syndrome (RDS) requiring surfactant within six hours of life were enrolled. Exclusion criteria included neonates who were intubated in the delivery room, babies with severe congenital anomalies, babies whose parents did not provide consent for their participation in the study. Inborn babies satisfying the eligibility criteria were provided delivery room CPAP using T-piece resuscitator. After shifting to the inborn unit, the baby was connected to nCPAP using appropriate sized Hudson prongs. Babies received surfactant by LISA when the fraction of inspired oxygen (FiO_2) requirement was more than 30% on CPAP with a pressure of 6 cm of water. Babies were alternately assigned to each arm. In group A (LISA-OG), a 5 F infant feeding tube was used to administer surfactant. While the infant was breathing via nCPAP, a direct laryngoscope was introduced to visualize vocal cords. Size 5 feeding tube was introduced and negotiated 2 cm below the vocal cord without the help of Magill forceps (similar to Take care method).[11] After fixing the catheter with the finger and ensuring the mouth of the neonate is closed, surfactant was administered over 2 minutes. In group B (LISA-ET), surfactant was administered using a 2 mm un-cuffed endotracheal (ET) tube while the neonate was breathing via nCPAP. The adapter of the ET tube was removed and the hub of the syringe barrel was directly attached to the outer end of the ET tube (Fig.1) and the surfactant was instilled over 2 minutes.[12]

Fig1. Showing administration of LISA using 2 size un-cuffed Endotracheal tube



In both the groups, caffeine at 20 mg / kg loading dose was used as a premedication and the surfactant used was Survanta at 100 mg / kg / dose. There was no premedication used for sedation or analgesia. Surfactant was administered by two doctors and a nurse was also present to record the events. A second dose of surfactant if needed was administered using INSURE technique. The primary outcome analyzed was the successful administration of surfactant using LISA-OG or LISA-ET without the need for PPV during the procedure. If the neonate developed bradycardia (HR < 100 / min), or apnea (SpO_2 < 80%), the procedure was halted, and PPV was given using a T-piece resuscitator for at least 1 min before considering a second attempt. If the catheter could not be negotiated below the vocal cords within 30 seconds of laryngoscopy, second attempt of laryngoscopy was performed after a gap of 1 min duration, during which respiratory support was continued. Secondary outcomes analyzed were hospital course-related outcomes with the help of the following indicators like the need for a second dose of surfactant, duration of respiratory support, duration of hospital stay, the incidence of bronchopulmonary dysplasia (BPD), patent ductus arteriosis (PDA) requiring medical closure, Necrotising enterocolitis (NEC) > stage 1, intraventricular haemorrhage (IVH) > grade II, retinopathy of prematurity (ROP) requiring laser therapy, and sepsis (Defined as culture-positive sepsis). As there are no previous studies addressing this research question, sample size was calculated by comparison of proportions, based on the event rate – apnea or bradycardia requiring positive pressure ventilation during intubation (0.1) and LISA-OG (0.45) from our unit experience. With 1:1 allocation in each arm, the desired sample size was 25 in each arm. Data recorded were analyzed using the SPSS software version 21.0 (SPSS, Chicago, IL). Data were expressed as proportion, mean (± standard deviation), or median (Interquartile range). Proportions were compared by the Chi-square test. Continuous variables were compared by Student's t-test or Mann-Whitney U test as per their distribution. A 'p' value < 0.05 was considered statistically significant.

Results

During the study period a total of 50 babies were enrolled, 25 in each arm. The flow diagram of the study population is shown in Fig. 2. Baseline characteristics of the study population are depicted in Table 1. Neonates in both arms were comparable in their baseline characteristics. The primary outcome and secondary outcomesare depicted in Table 2. Administration of LISA using a 2 mm ET tube was associated with the better success of surfactant administration (80% vs. 44%, RR-1.8) with lesser incidence of PPV need, desaturation (20% vs. 48%, RR – 0.4), and bradycardia (12% vs. 40%, RR – 0.3) with a significant p-value. More than one attempt was needed for the successful negotiation of the catheter below the vocal cords in 13 / 25 neonates among LISA-OG compared to 3 / 25 neonates in the LISA-ET group.

Fig 2. Flow diagram of the study population

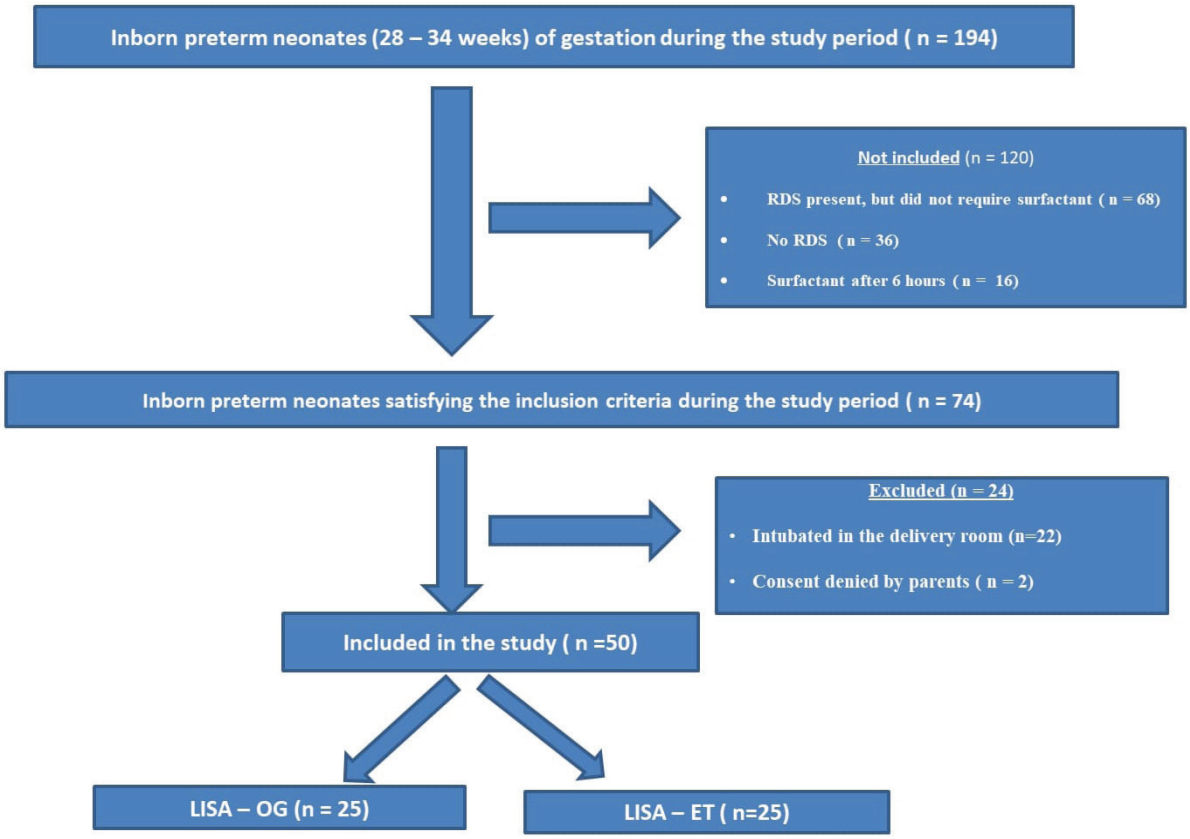


Table 1. Baseline characteristics of the study population

Characteristics	LISA – OG (n = 25)	LISA – ET (n = 25)
Male n (%)	12 (48%)	14 (56%)
Birth weight (g) Mean ± SD	215 ± 1120	245 ± 1140
Gestational age (weeks) Mean ± SD 28 – 30 weeks n (%) 31 – 34 weeks n (%)	30 ± 1.7 16 (64%) 9 (36%)	1.6 ± 29.8 14 (56%) 11 (44%)
Growth status at birth n (%) SGA (Small for gestational age) AGA (Appropriate for gestational age)	 7 (28%) 18 (72%)	 9 (36%) 16 (64%)
Maternal age (years) Mean ± SD	4.5 ± 24.6	3.3 ± 26.2
Complete course of antenatal corticosteroids received n (%)	(32%) 8	9 (36%)
Mode of delivery n (%) Vaginal Caesarean section	 16 (64%) 9 (36%)	 15 (60%) 10 (40%)
Surfactant timing – n (%) ERST (Early rescue surfactant therapy) LRST (Late rescue surfactant therapy)	 22 (88%) 3 (12%)	 21 (84%) 4 (16%)

Table 2. Table depicting the primary outcome and secondary outcomes

Indicator	LISA – OG (n = 25)	LISA – ET (n = 25)	p- value
Primary outcome			
Successful attempts of surfactant administration without any need for PPV during the procedure n (%)	11 (44%)	20 (80%)	< 0.05*
Bradycardia (HR< 100/min) n (%)	10 (40%)	3 (12%)	< 0.05*
SpO2 < 80% - n (%)	12 (48%)	5 (20%)	< 0.05*
More than one attempt needed for successful negotiation of catheter below the vocal cords – n (%)	13 (52%)	3 (12%)	< 0.05*
Secondary outcomes			
Need for second dose of surfactant –n	3	1	
Need for mechanical ventilation in the first 72 hours of life -n	5	3	0.26
Total duration of non-invasive ventilation during hospital stay (days) – Median (25^{th}- 75^{th} IQR)	9 (5.6 -14.3)	8 (6.3 -15.2)	0.15
Pneumothorax – n	-	-	
BPD – n	2	1	
Culture positive sepsis – n	6	8	0.29
Intraventricular haemorrhage (IVH) > grade 2 – n	2	1	
Periventricular leucomalacia (PVL) – n	1	1	
Necrotising enterocolitis (NEC) ≥ stage 2 – n	1	0	
Retinopathy of prematurity requiring laser therapy – n	1	1	
Patent ductus arteriosus requiring medical closure – n	3	4	
Duration of hospital stay (days) Mean ± SD	30.8 ± 11.2	31.3 ± 12.6	0.22

*-significant p-value

Discussion

LISA though has multiple benefits as demonstrated in various trials, is a technically demanding intervention requiring practice and expertise to reap the best out of it. In our study (Table 2), LISA-ET was associated with a higher incidence of successful surfactant administration (80% vs. 44%) with lesser incidence of the need for PPV, bradycardia (12% vs. 40%), and desaturation (20% vs. 48%) compared to LISA-OG arm. In an Indian study comparing INSURE and SURE (Surfactant without endotracheal tube), a higher incidence of apnea and bradycardia during the procedure were noted in the SURE arm where a thin catheter was used with no such events being documented in the INSURE arm where ET tube was used.[13] Though INSURE (Intubate, Surfactant, and Extubate) is a time-tested, well-tolerated, and easy to perform technique, the need for few mechanical breathes increases the risk of BPD. Where there arises a need for PPV during LISA, it loses its essence of being a gentler modality in the true sense. Evidence suggests that the number of attempts used for thin catheter technique is not significantly different among various studies, but there exists a paucity of data from India.[14] In our study (Table 2), the need for more than a single attempt for successful negotiation of catheter below the vocal cords was higher in LISA-OG (52%), compared to LISA-ET (12%). Longer duration of a technically difficult procedure with multiple attempts of laryngoscopy may lead to discomfort in the neonate causing apnea or bradycardia, thereby leading to a higher incidence of PPV and unsuccessful attempts. The concern is even more in an academic institute like ours, where the LISA procedure would be performed by multiple doctors who may differ in their technical skills. To retain the benefits and avoid the above-mentioned adverse events, we innovated to use the smallest available ET tube for the administration of surfactant by LISA.

Feeding tubes are the most frequently used catheters for LISA. Sizes ranging from 5 F to 8 F were used by various units as per their convenience. Few units even practiced freezing the feeding tubes before the procedure to enhance their stiffness. However, feeding tubes are made up of polyurethane (PU) material, and hence lacks the firmness needed for easy maneuvering. On the other hand, the traditional ET tubes are made up of polyvinyl chloride material, which imparts rigidity and facilitates the ease of insertion.[12] This is evident from the result of our study where LISA administration using feeding tube required more attempts for successful surfactant instillation. Also, the higher incidence of apnea and bradycardia in the feeding tube arm could probably be explained by the need for increased time and attempts to maneuver the feeding tube between the vocal cords into the trachea leading to distress in the baby. The need for a second dose of surfactant would indirectly indicate more wastage of surfactant due to reflux or displacement

of the thin feeding tube during administration.

LISA is a gentler technique based on the concept to minimise tracheal instrumentation. The trauma due to tracheal instrumentation could be quantitative (the duration of instrumentation), or qualitative (based on the size of the catheter used).[12] The currently available smallest endotracheal tube (size 2) has an outer diameter of 2.7 mm which is equivalent to an 8 F feeding tube. However, the catheter used routinely for LISA is a 5 F feeding tube which has an outer diameter of 1.7 mm. The purpose of our study lies to answer the question of whether this difference of 1 mm is significant to cause an impact on the outcome. As evident from the results of our study, there was an ease of surfactant administration noted in the LISA-ET arm with a better success rate and lesser incidence of PPV need, bradycardia, and apnea, and no difference in other hospital related outcomes compared to the LISA-OG arm. The above results highlight that, not just the size of the catheter, but the duration of instrumentation plays a pivotal role in a successful LISA therapy.

To the best of our knowledge, this is the first study to address and compare the success rate, ease of administration of LISA using 2.0 ET and 5 F feeding tube. The use of 2.0 ET was an innovation born out of practical and technical difficulty faced for the administration of LISA using thin catheters. Only when we performed a literature search at a later date, we came across a case report where a similar technique was used.[12] There is potential scope for this innovation in resource-limited countries where commercially available LISA catheters cannot be used due to high costs. This was a pilot study attempting to generate a hypothesis. There is a need for well-powered, good numbered, randomized control trials to test this easily adaptable technique of LISA. We acknowledge the following limitations to our study – a small sample size, not being a randomized trial, not including extremely premature neonates.

Conclusions

In conclusion, the results from our study suggests that the use of anuncuffed 2.0 mm ET tube could be an easier and convenient way to successfully administer surfactant compared to a 5 F feeding tube with lesser incidence of apnea and bradycardia and need for PPV during the procedure. The baby gets the benefit of LISA with better tolerability, without any adverse hospital course-relatedoutcomes compared to the use of a 5 F feeding tube.

References

1. 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: 432-50. DOI: 10.1159/000499361.
2. Gengaimuthu K: Should minimally invasive surfactant therapy be a must in neonatal intensive care units? Pilot report of initial cases in Dubai. Cureus. 2018; 10:3495. DOI:10.7759/cureus.3495.
3. Rigo V, Lefebvre C, Broux I. Surfactant instillation in spontaneously breathing preterm infants: a systematic review and metaanalysis. Eur J Pediatr. 2016;175(12):1933–42. DOI: 10.1007/s00431-016-2789-4.
4. 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;316(6):611–24. DOI: 10. 1001/jama.2016.10708.
5. Lau CSM, Chamberlain RS, Sun S. Less Invasive Surfactant Administration Reduces the Need for Mechanical Ventilation in Preterm Infants: A Meta-Analysis. Glob Pediatr Health. 2017;24(4):1-9. DOI: 10.1177/2333794X17696683. PMID: 28540346;
6. Aldana-Aguirre JC, Pinto M, Featherstone R, 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; 102(1):F17-F23. DOI: 10.1136/archdischild-2015-310299
7. Herting E, Härtel C, Göpel W. Less invasive surfactant administration: best practices and unanswered questions. Curr Opin Pediatr. 2020;32(2):228-34. DOI: 10.1097/MOP.0000000000000878.
8. Kribs A. Minimally Invasive Surfactant Therapy and Noninvasive Respiratory Support. Clin Perinatol. 2016;43(4):755-71. DOI: 10.1016/j.clp.2016.07.010.
9. Lista G, Bresesti I, Fabbri L: Is less invasive surfactant administration necessary or 'only' helpful or just a fashion. Am J Perinatol. 2018; 35(6):530-33. DOI:10.1055/s-0038-1637759.
10. Rigo V, Debauche C, Maton P, Broux I, Van Laere D. Rigid catheters reduced duration of less invasive surfactant therapy procedures in manikins. Acta Paediatr. 2017; 106(7):1091 -96. DOI: 10.1111/apa.13850.
11. Kanmaz H, Erdeve O, Canpolat F, Mutlu B, Dilmen U. Surfactant Administration via Thin Catheter During Spontaneous Breathing : Randomized Controlled Trial. Pediatrics; 131(2): e502-e509. DOI: 10.1542/peds.2012-0603
12. Gengaimuthu K. Minimally Invasive Surfactant Therapy Using a 2.0 mm Uncuffed Endotracheal Tube as the Conduit: An Easily Adaptable Technique. Cureus 2019;11(8):e5428. DOI: 10.7759/cureus.5428.
13. Jena SR, Bains HS, Pandita A,Verma A, Gupta V, Kallem V R, et al. Surfactant therapy in premature babies: SurE or InSurE. Pediatr Pulmonol. 2019;54(11):1747-52. DOI: 10.1002/ppul.24479.
14. Devi U, Pandita A. Surfactant delivery via thin catheters: methods, limitations, and outcomes. Pediatr Pulmonol. 2021;1-16. DOI: 10.1002/ppul.25599