

Introducing LISA: Less Invasive Surfactant Administration

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Abstract

Aim

Less Invasive Surfactant Administration (LISA) is now an established method of surfactant delivery for the treatment of Respiratory Distress Syndrome (RDS) in preterm neonates. It has been widely adopted in Europe, but the uptake of LISA in the UK and USA has been much slower. The purpose of this study is to report on the experience of LISA introduction to our Level 2 neonatal unit, and to determine the proportion of neonatal units currently using LISA in the Ireland.

Methods

Retrospective descriptive audit of infants who had received surfactant via LISA in our unit from its introduction in February 2018 to March 2022, and a nationwide online survey, to quantify the national prevalence of LISA use.

Results

Over the four-year period, 104 infants received surfactant via LISA. Over 75% of infants received surfactant via LISA in 2022, compared to less than 20% in 2018. Our nationwide survey demonstrated a low uptake of LISA, with only 26% of Irish units using LISA.

Discussion

Our study demonstrated that LISA can be safely and successfully introduced to a Level 2 neonatal unit. Our national survey identified a low uptake of LISA. The slow uptake of LISA in the Ireland may be attributed to a lack of familiarity with the LISA technique.

Introduction

Less Invasive Surfactant Administration (LISA) is now an established method of surfactant delivery for the treatment of Respiratory Distress Syndrome (RDS) in preterm neonates¹. LISA is considered the preferred mode of surfactant administration for spontaneously breathing infants on Continuous Positive Airway Pressure (CPAP), with benefits including less need for mechanical ventilation and a reduced incidence of BPD and death at 36 weeks². It has been widely adopted in Europe, but the uptake of LISA in the UK and USA has been much slower³⁻⁵.

Little is known about the use of LISA in the Ireland, a country with 19 neonatal units and a birth rate of 65,000. In February 2018, we became the first Irish neonatal unit to introduce the LISA technique as the standard method of surfactant delivery in our Level 2 neonatal unit. The objective of this study was to examine our experience with LISA between February 2018 and March 2022, and to determine the uptake of LISA in Ireland.

Methods

In February 2018, Galway University Hospital (GUH) commenced using the LISA technique as the standard method of surfactant delivery. GUH is a regional Level 2 Neonatal Intensive Care Unit (NICU), with over 400 admissions per year, providing care for preterm infant's ≥ 27 weeks gestation. The study was approved by the Galway University Hospital (GUH) Ethics Committee (Reference No: C.A. 2924).

Babies with evolving RDS were administered early rescue surfactant (Poractant alfa) at dose of 200 mg/kg via LISA. Clinical criteria for LISA included: fraction of inspired oxygen (FiO₂) requirement $\geq 30\%$ on Continuous Positive Airway Pressure (CPAP); clinical signs of increased work of breathing, such as tachypnoea and sternal recession; and/or radiological evidence of RDS⁶⁻⁷.

LISA was performed by a Neonatal Registrar, Advanced Nurse Practitioner (ANP) or Neonatal Consultant. Sucrose was used as the standard premedication. Infants self-ventilated on supplemental oxygen delivered by nasal Continuous or Bilevel Positive Airway Pressure (CPAP or BiPAP) during the procedure. Tracheal catheterization was achieved almost exclusively by video-laryngoscopy. Clinicians utilised a semi-rigid catheter: either a LISAcath (Chiesi Farmaceutici S.p.A.; Parma, Italy) or a Surfath (Vygon SAS; Écouen, France). Surfactant was delivered gradually over 2-5 minutes, to minimise the risk of desaturation or bradycardia.

All babies who had received surfactant via LISA, from February 2018 to March 2022, were audited. Data was collected retrospectively from handwritten patient notes and the Electronic Patient Record (EPR). LISA patient characteristics, associated events and early clinical outcomes were recorded.

We also carried out a nationwide survey to quantify the prevalence of LISA use in Irish neonatal units. This online survey was completed by local clinicians in May 2022 (Appendix 1). Where necessary, a follow-up phone interview was performed for clarification of clinical practice.

Results

During the study period, February 2018 to March 2022, 104 infants received surfactant via LISA in our neonatal unit.

The gestational age of the LISA infants varied from 25-41 weeks and birth weights ranged from 725 to 4460g. Most infants that received surfactant via LISA had been exposed to antenatal steroids (82%), and the majority were born via C-Section (78%). Almost all of the LISA infants were born in good condition (mean Apgar Scores 8 at 1 minute and 9 at 5 minutes). Most were placed on non-invasive respiratory support shortly after birth (Table 1).

Table 1: Patient characteristics of neonates who received LISA

Total Neonates	n=104
Median birth weight, g (range)	1785 (725-4460)
Median gestational age, weeks (range)	31.8 (25-41)
Gestational Age	
Extremely Preterm (<28 weeks)	9 (9%)
Very Preterm (28 – 32 weeks)	44 (42%)
Moderately Preterm (32 – 35 weeks)	30 (29%)
Late Preterm (35 – 37 weeks)	14 (13%)
Term (>37 weeks)	7 (7%)
Antenatal Steroids	
Prevalence of administration	85 (82%)
Median doses received	2 (0-4)
Mode of Delivery	
Spontaneous Vaginal Delivery (SVD)	24 (22%)
Lower Segment Caesarean Section (LSCS)	82 (78%)

APGAR score	
1 minute (range)	8 (2-9)
5 minutes (range)	9 (2-10)
10 minutes (range)	9 (2-10)
Respiratory Support at Delivery	
Spontaneous Ventilation on Room Air (SVRA)	3 (3%)
Continuous Positive Airway Pressure (CPAP)	71 (68%)
Intermittent Positive Pressure Ventilation (IPPV)	29 (28%)
Intubation and Ventilation	1 (1%)

Within four years of introducing the procedure, LISA had become the dominant surfactant administration method, with over 75% of infants in 2022 receiving surfactant via LISA (Figure 1).

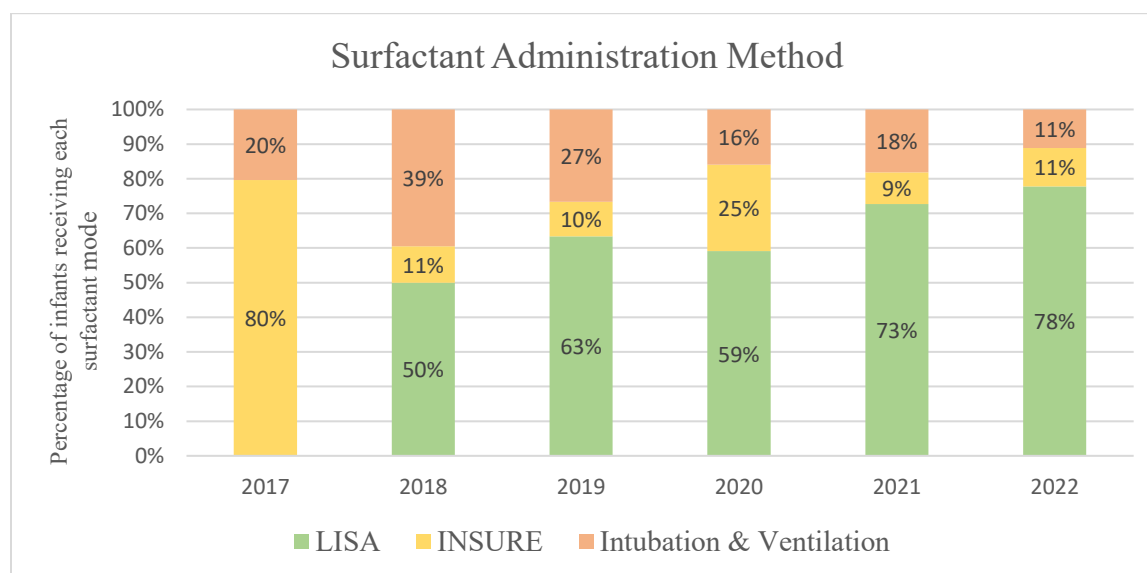


Figure 1: GUH Surfactant Administration Method 2017-2022

LISA was performed in the Neonatal Unit by a neonatal registrar in 78% of cases, an advanced nurse practitioner in 15%, and a neonatal consultant in the remaining 7%. Infants received their first dose of surfactant at a mean of 2 hours of life. Following LISA, the median FiO₂ decreased from 40% pre-procedure to 25% at 6 hours post-procedure. LISA-associated adverse events included: 11% of infants required repeat surfactant administration, 6% developed a pneumothorax and 5% had failure of treatment, defined as the need for mechanical ventilation within 72 hours of the LISA procedure (Table 2).

Table 2: Early clinical outcomes of neonates who received LISA

Total Neonates	n=104
LISA Procedure	
Median age at time of procedure, hours of life (range)	2 (0.08 - 98)
Median pre-procedural oxygen requirement (FiO ₂ %) (range)	40% (21-90%)
Median post-procedural oxygen requirement (FiO ₂ %, at 6 hours) (range)	25% (21-70%)
Median dose of surfactant, mg/kg (range)	200 (100-200)
Median number of attempts (range)	1 (1-6)
Clinician performing LISA	
Neonatal Registrar	80 (78%)
Advanced Nurse Practitioner	15 (15%)
Neonatal Consultant	7 (7%)
LISA-Associated Events	
Infants requiring repeat surfactant administration	12 (12%)
Median quantity of repeat doses (range)	1 (1-2)
Pneumothorax	6 (6%)
Failure (mechanical ventilation within 72 hours of LISA procedure)	6 (5%)

Our nationwide survey collected responses from all 19 Irish neonatal units (Table 3), and included four tertiary units (Level 3), four regional units (Level 2) and 11 local units (Level 1).

Table 3: LISA in Neonatal Units in Ireland in 2022 (Online survey)

Total Neonatal Units in Ireland	n=19
Unit level	
Level 1	11 (58%)
Level 2	4 (21%)
Level 3	4 (21%)
Frequency of surfactant administration in the unit per year	
<10 times	8 (42%)

11-40 times	8 (42%)	
41-60 times	3 (16%)	
Methods of Surfactant Administration (Often many)		
INSURE	13 (68%)	
LISA	5 (26%)	
Intubation and mechanical ventilation	11 (58%)	
Has LISA ever been used in the unit?		
yes	5 (26%)	
no	14 (74%)	
Number of Level 3 units using LISA	1 (25%)	
Number of Level 2 units using LISA	2 (50%)	
Number of Level 1 units using LISA	2 (18%)	
Median duration of LISA experience (years)	2 (1-6)	
Is LISA the primary method of surfactant administration in the unit?		
Yes	2/5	Eight units

(42%) units had <10 annual surfactant administrations, another 8 units (42%) gave surfactant 11-40 per year, while the remaining 3 units (16%) carried out 41-60 surfactant administrations each year. The majority of units (13/19) performed INSURE, many in conjunction with other methods.

Only 5 of 19 (26%) Irish neonatal units used LISA as a method of administering surfactant: one tertiary unit, two regional units, and two local units. Only 2 of the 5 units using LISA (40%) reported that it was their primary method of surfactant administration.

Table 4: LISA in neonatal units in Ireland in 2022 (Online survey)

Total Neonatal Units in Ireland	n=19
Preferred gestational age for use of LISA	
>26 weeks	1 (20%)
>27 weeks	1 (20%)
>36 weeks	1 (20%)
None specified	2 (40%)
FiO2 Threshold for Surfactant via LISA	
≥0.3	3/4 (75%)
≥0.4	1/4(25%)

Who can perform LISA?	
Consultant	5 (100%)
Registrar	4 (80%)
Advanced Nurse Practitioner	2 (40%)
Senior House Officer	1 (20%)
Devices used to administer LISA	
LISAcath	4 (80%)
Feeding tube catheter	1 (20%)
Use of sedation/premedication	
Yes	2 (40%)
No	3 (60%)
Policy for use of LISA?	
Yes	2 (40%)
No	3 (60%)
Reasons for not using LISA	
Unfamiliar with Technique	7/14 (50%)
Not Evidence Based	3/14 (22%)
Other	4/14 (28%)

There was a wide variation in the local criteria for LISA administration: based on FiO₂ requirement and gestational age (Table 4). Two units (40%) used either a traditional or a video laryngoscope to visualize the vocal cords, while the remaining three units (60%) used a video laryngoscope only. Eighty percent (4/5) of units used a LISAcath, while 20% (1/5) used a feeding tube catheter. The vast majority (3/5) did not use any sedation/premedication. One unit used sucrose as a premedication whilst another reported ketamine and occasionally fentanyl use. Only 40% of units reported having a protocol for the use of LISA.

For units not using LISA (14/19), the most common reason cited was an unfamiliarity with the technique (7/14), while 22% felt that there was inconclusive evidence regarding LISA. The majority (57%) of the neonatal units not using LISA said they would consider use of LISA in the future, while 13% of units said had no plans to use LISA.

Discussion

This retrospective descriptive audit reports on the introduction of LISA to a Level 2 Irish neonatal unit. Over a four-year period LISA became the dominant method of surfactant delivery in our unit, with over 75% of infants receiving surfactant via LISA in 2022. This compares to less than 20% on its introduction in 2018. Similar progress with the introduction of this less invasive

surfactant administration technique has been reported in many European countries, including Belgium, where a recent nationwide survey of neonatologists (n=102, response rate 86%) reported that the majority of late preterm infants with Hyaline Membrane Disease (HMD) in 2020 were administered surfactant via LISA (56%).

The European Consensus Guidelines on the Management of Respiratory Distress Syndrome 2019 update recommended, for the first time, LISA as the preferred mode of surfactant administration for spontaneous breathing infants on CPAP, provided that local clinicians were familiar with the technique. This recommendation was based on data from studies and meta-analyses comparing surfactant administration methods, that were published subsequent to the 2016 version of the Consensus Guidelines, and suggested that LISA was superior to other surfactant administration modes in terms of reducing the need for mechanical ventilation, and the combined outcome of death and BPD⁶. However, even prior to the 2019 endorsement of LISA by the European Consensus Guidelines group the procedure had already been widely adopted by neonatal units throughout Europe, with an online survey of 37 European countries in early 2016 reporting that 52% of neonatal units were performing LISA.

Our national survey demonstrated that LISA usage remains low in the Ireland in 2022, with only 26% of Irish neonatal units have ever practised LISA. While it may be understandable that Level 1 units, which lack specific expertise in neonatal care and very infrequently administrate surfactant, have not adopted LISA, it is surprising, and out of keeping with neonatal unit practices throughout Europe, that more of the units that have neonatal expertise and commonly administer surfactant have not adopted the LISA technique. In our survey, a lack of familiarity with the LISA technique and a belief that the procedure was not evidence based were cited as reasons for not performing the procedure. The general decline in the use of invasive neonatal ventilation, due to non-invasive methods such as CPAP and BiPAP, may also have contributed to the slow adaption of LISA use in Ireland⁸. Trainees now have few opportunities to develop endotracheal intubation skills, which can be invaluable in a neonatal resuscitation scenario, and a belief exists that continuing to administer surfactant via the INSURE method, rather than pivoting to LISA, will at least preserve some of the non-emergency opportunities for placing an endotracheal tube in the airway.

A video laryngoscope provides an indirect view of the airway, and live visualization of airway procedures, on a video screen that can be observed by multiple trainees, and it is an invaluable tool for training in neonatal airway procedures⁹. In our unit a video laryngoscope, rather than a standard laryngoscope, was used to assist in positioning of the LISA catheter. Studies have demonstrated that the video laryngoscope promotes the development of intubation skills among trainees⁹. It improves the success rate on first attempt of ET placement, and reduces the risk of

intubation-related trauma, which is more prevalent with multiple or prolonged attempts¹⁰. It is likely the success of our LISA program was in part due to the use of the video laryngoscope, which greatly facilitated training staff in the procedure. In our opinion, units considering adopting the LISA procedure should use a video laryngoscope, to assist in training and successful catheter placement.

In summary, LISA has been endorsed by the European Consensus Guidelines group as the preferred mode of surfactant administration for spontaneous breathing infants on CPAP, and the procedure has been widely adopted throughout neonatal units in most European countries. LISA became the dominant method of surfactant delivery in our unit within four years of introduction. However, other neonatal units in Ireland have been slow to adopt this less invasive surfactant administration technique. The low use of LISA in Irish neonatal units seems to be related to a satisfaction with current surfactant delivery methods and a general lack of enthusiasm to introduce LISA, possibly due to concerns about deskilling.

Declarations of Conflicts of Interest:

None declared.

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