Yorkshire & Humber Network Neonatal Clinical Guideline (PAN)

Title: Surfactant administration for Respiratory Distress Syndrome

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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire and Humber Neonatal ODN. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Best practice recommendations represent widely used evidence-based practice and high quality standards that all Neonatal Units across the Network should implement. Subsequent suggested recommendations may be put into practice in local units. However, alternative appropriate local guidelines may also exist.

A. Guideline summary

1. Aims

To provide evidence-based, best practice guidance for use of surfactant in respiratory distress syndrome, across the Yorkshire and Humber Neonatal ODN.

1. Best Practice Recommendations

2. Guideline Summary

B Full guideline and evidence

1. Background

Benefits of Surfactant

Pulmonary surfactant is a mixture of phospholipids and proteins which are normally produced by type II pneumocytes. One of its main functions is to reduce surface tension in the alveoli, preventing atelectasis.

Respiratory distress syndrome (RDS), also known as hyaline membrane disease or surfactant-deficient lung disease, is mainly a disease of preterm infants that results from a lack of pulmonary surfactant. It is characterised clinically by hypoxia and/or respiratory distress that may get worse over the first 48 hours, and radiographically as underinflation, “ground-glass” appearances and air bronchograms. Multiple meta-analyses have shown exogenous surfactant therapy to be beneficial in managing RDS in conjunction with respiratory support; both non-invasive and mechanical ventilation. These benefits include reduced need for ventilation, reduced mortality, bronchopulmonary dysplasia and pneumothorax.

Although unrelated to this guideline, exogenous surfactant has also been shown to reduce disease progression and need for ECMO in infants with meconium aspiration syndrome. There is no evidence to support the administration of surfactant via less invasive means e.g. LISA for babies with meconium aspiration syndrome.

2. Aim

To provide evidence-based, best practice guidance for use of surfactant in respiratory distress syndrome, across the Yorkshire and the Humber Neonatal ODN. Areas covered include:

- Less Invasive Surfactant Administration (LISA)
- INtubate SURfactant Extubate (INSURE)

3. Areas outside remit

Surfactant administration in conditions other than RDS

4. Evidence

4.1 Approaches and dose of surfactant

Traditionally, surfactant was given prophylactically to at-risk infants following intubation and ventilation. Following improvements in antenatal steroid exposure and immediate, delivery-room CPAP, prophylactic surfactant seems to be associated with increased mortality and bronchopulmonary dysplasia (BPD) compared to a more selective approach[i]. Evidence suggests that an "early rescue" approach, in which exogenous surfactant is delivered early in the disease progression of RDS, in the first 2-5 hours of life, should be preferred in infants that are spontaneously breathing on CPAP. This is in line with the European Consensus Guideline on the Management of RDS 2019[ii].

Animal-derived surfactants are more extensively studied and should be used for RDS. Most units in the UK use porcine-derived poractant alfa (Curosurf). At an initial dose of 200mg/kg, poractant alfa has been shown to reduce need for further surfactant administration and may improve survival against both 100mg/kg of beractant or 100mg/kg of poractant alfa[iii,iv].

The European Consensus Guideline on the Management of RDS recommends a dose of 200mg/kg for early rescue surfactant. Additional doses are usually given at 100mg/kg and usually after 12 hours.

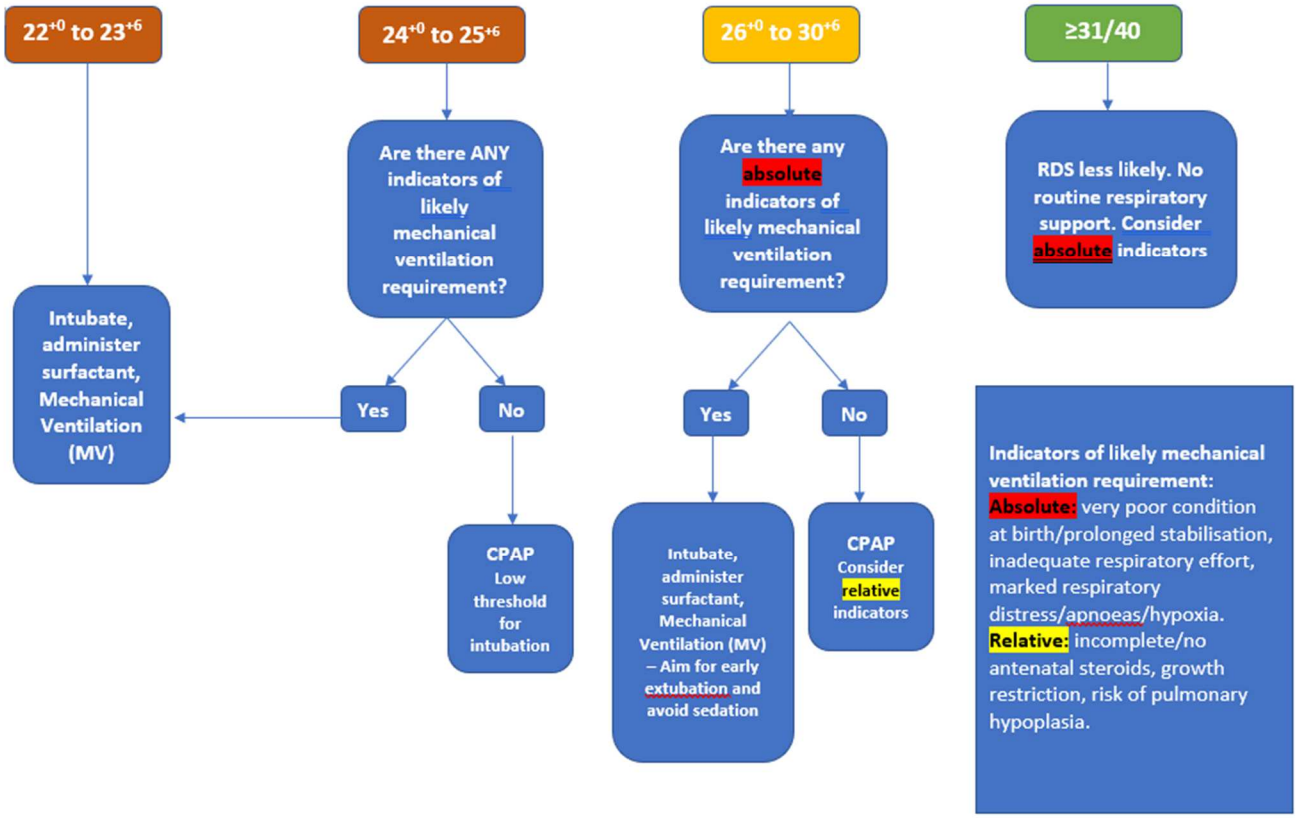
Concerns regarding the role of positive pressure ventilation in the development of BPD, and other adverse outcomes, have made clinicians keen to explore less invasive methods of surfactant delivery. The two methods which are most extensively practised and studied are INSURE (INtubate SURfactant Extubate) and LISA (Less Invasive Surfactant Administration). A recent Cochrane review[v] found that, when compared to administration of surfactant via endotracheal tube e.g., INSURE, LISA resulted in a decreased risk of BPD/death at 36 weeks (RR 0.59, CI 0.48-0.73, NNTB 9), reduced need for intubation at 72 hours (RR 0.63, CI 0.54-0.74) and reduced risk of severe IVH (RR 0.63, CI 0.42-0.96), with no increased risk of air leak.

Please see below a decision tree to help decide which method of respiratory support and/or surfactant administration would be routine for infants with RDS at different gestational ages and with varying clinical conditions.

4.1 Decision tree for surfactant administration

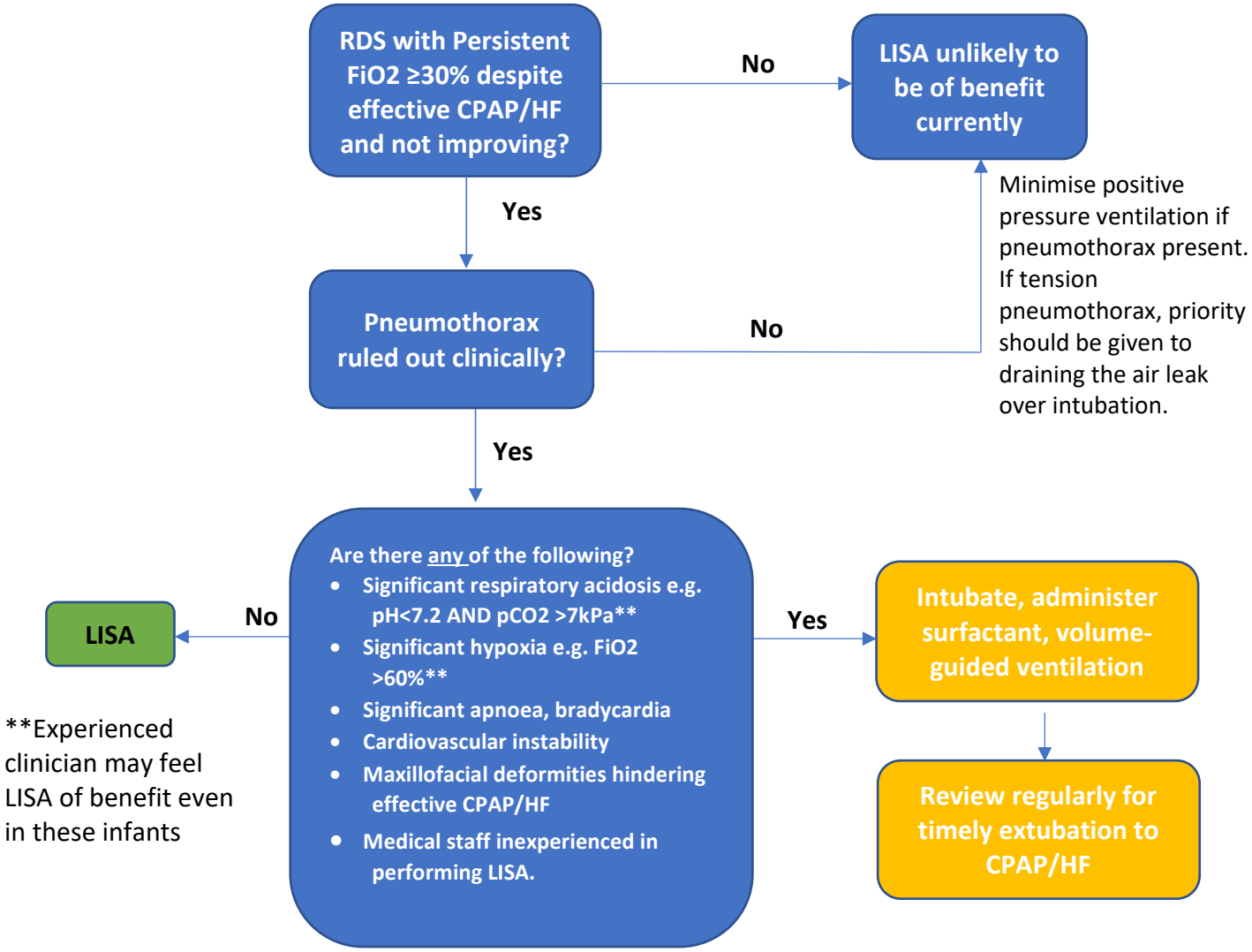
At birth

- the following approaches would be considered routine management. However, each case should be considered individually.



If the infant will require imminent **Embrace transfer** from your unit, please consider routine intubation and mechanical ventilation, rather than LISA. This could be on the neonatal unit in more controlled conditions.

On Neonatal unit – Within first 2 hours of life, if an infant has RDS and remains on CPAP/HF consider the following treatment algorithm:



4.2 Less Invasive Surfactant Administration (LISA)

4.2.1 Eligibility Criteria

Infants that will benefit from LISA are those with evolving RDS, who are breathing spontaneously. RDS can be diagnosed clinically in at-risk infants. As the risk of RDS decreases with increasing gestational age, it would be appropriate to confirm the diagnosis of RDS radiologically in infants over 32 weeks. A threshold of FiO2 30% at or before 2 hours of life, in an infant receiving effective High Flow (HF) therapy or effective CPAP (at or above 6cmH_2O) is a reasonable threshold for early rescue surfactant therapy.

4.2.2 Exclusion Criteria

LISA is not appropriate for all infants with RDS. In these infants, routine intubation, administration of surfactant and volume-guided ventilation should be undertaken. Extubation at the earliest, safe opportunity should be considered.

Careful consideration must be made to the following:

- How likely is the infant to remain stable on non-invasive respiratory support?
    - Most neonatal units within our region would routinely intubate infants less than 24+6 weeks gestation if they show signs of evolving RDS, as opposed to attempting LISA
    - Infants with very severe RDS, defined by very high oxygen requirements (e.g., >60% oxygen), marked apnoeas/bradycardias and/or significant respiratory acidosis are unlikely to manage without intubation, therefore LISA may not be appropriate
    - Infants who are cardiovascularly unstable are more likely to require intubation and mechanical ventilation
    - Low birth weight, lack of antenatal steroids, risk factors for pulmonary hypoplasia such as prolonged rupture of membranes/oligohydramnios and significant sepsis will increase the risk of an infant ultimately requiring mechanical ventilation and should be considered before performing LISA
    - More mature, more vigorous infants may not tolerate the LISA procedure with no or minimal sedation.
- What is the experience level of performing LISA of the staff present?
- Will the infant require Embrace transfer imminently?
    - LNUs should only perform LISA on infants that are likely to remain within their unit. If the infant is likely to need Embrace transfer (capacity, low gestational age, low birthweight, multi-organ impairment) then intubation, surfactant administration and mechanical ventilation may be more appropriate.
- Are there any maxillofacial anomalies that would preclude effective CPAP/High Flow?
- **There have been a number of risk incidents regionally involving LISA given to infants with pneumothoraces. LISA is not appropriate in the context of an undrained pneumothorax and this should be ruled out clinically or radiologically first.**

There is no evidence to support LISA as a method of administering surfactant in the context of meconium aspiration syndrome.

4.3.3 Personnel

Before commencing the procedure, LISA should be discussed with the consultant neonatologist on-call to ensure that LISA is appropriate, that there are no contra-indications and to provide advice/assistance. It would be appropriate for medical staff in an LNU to discuss cases with their regional NICU consultant before attempting LISA in atypical cases such as infants of more than 36 weeks gestation.

LISA should only be performed by health professionals that are proficient in endotracheal intubation. They must have experience in LISA or be supervised by an experienced LISA practitioner.

4.3.4 Pre-procedure

Preparation for the procedure is essential in achieving the best results.

- Has RDS been confirmed clinically? (Consider chest x-ray if >32^{+0} weeks GA)
- Has a pneumothorax been ruled out clinically/radiologically?
- Is the infant receiving effective CPAP/HF?
- Ensure patient is monitored – HR/oxygen saturations/temperature
- Consider thermoregulation – increase ambient temperature, hat, blankets and consider transwarmer mattress
- Have they received a caffeine loading dose (as per local unit's policy)? – Do not delay surfactant but aim to give loading dose of caffeine at first available opportunity.
- Do they have working IV access?
- An NGT/OGT in situ may help identify cords, reduce gastric insufflation and also identify oesophageal administration of surfactant post-procedure
- Ensure immediate surroundings and patient position are optimised - consider raising head end of bed slightly to promote gravity avoidance of reflux of surfactant following administration.
- Aim to maintain effective non-invasive ventilation (with PEEP/CPAP) throughout the procedure
- Consider good neurodevelopmental care – nest, swaddle, buccal EBM/sucrose
- If situation allows, inform parents

4.3.5 Equipment

- Checklist (see Appendix A)
- Laryngoscope
    - A video laryngoscope is preferred for all LISA attempts as it assists in training, in addition to allowing the whole team see the catheter pass through the cords, ensuring appropriate placement. If LISA is being performed by an inexperienced practitioner under supervision, then a video laryngoscope should be considered mandatory.
- Surfactant (Curosurf) 200mg/kg, at room temperature
- Appropriate surfactant catheter (e.g. LISAcath, Surfcath)
    - Consider putting slight bend on the catheter.
    - Consider putting Steristrip at estimated length as visual guide for team e.g. weight in kg + 6 cm as an estimate for length at the lips.
- 5ml Luerlock syringe **(please note ENFIT giving set is not compatible with surfactant catheter).**
    - In order to prevent risk of other drugs being inadvertently delivered via the LISA catheter it is essential that the equipment for performing LISA is on a separate trolley/tray to that of the drugs and flush being delivered intravenously. Best practice would be to label all medication syringes including the surfactant.
    - Consider attaching a Luerlock extension to the surfactant catheter as this reduces traction on the catheter when attaching the syringe and administering the surfactant
- T-piece mask inflation circuit with appropriate pressures set
- Appropriately sized face mask
- Equipment for ventilation
- Suction catheters and suction ready
- Intubation pre-medications drawn up and labelled (please note that surfactant may look like propofol when drawn up in a syringe)

4.3.6 Pre-medication

Sedation should be considered in all infants and may be particularly important in more mature infants e.g., >32 weeks GA to improve likelihood of a successful procedure. Good neurodevelopmental care should be employed for all patients receiving LISA including swaddling and buccal EBM/sucrose.

The most frequently used medication for sedation during LISA is the rapid-acting opiate fentanyl. Units across the region have used a dose range between 0.5micrograms/kg and 0.75micrograms/kg. Fentanyl may take 5-10mins to achieve peak effect but can be topped-up with a further dose of 0.5micrograms/kg after 10min. Fentanyl and its accompanied flush should be given very slowly to prevent chest wall rigidity. Some units use naloxone (20micrograms/kg) during the procedure once the laryngoscope has been removed to encourage spontaneous respiration.

Other units within the network have more experience using propofol for intubation and as such they use a quarter of their standard 2mg/kg dose i.e., 0.5mg/kg for LISA, with another dose to top-up if necessary. Propofol should be avoided in children with cardiovascular instability or congenital cardiac disease due to potential risk of hypotension. If using propofol, the syringe should be clearly labelled and placed on a separate trolley to avoid any confusion with the surfactant that is also drawn up.

Use of swaddling and/or sucrose alone in less mature infants can be considered by experienced personnel where intravenous access is not available or if the infant is settled. This may avoid the potential for respiratory depression during the procedure.

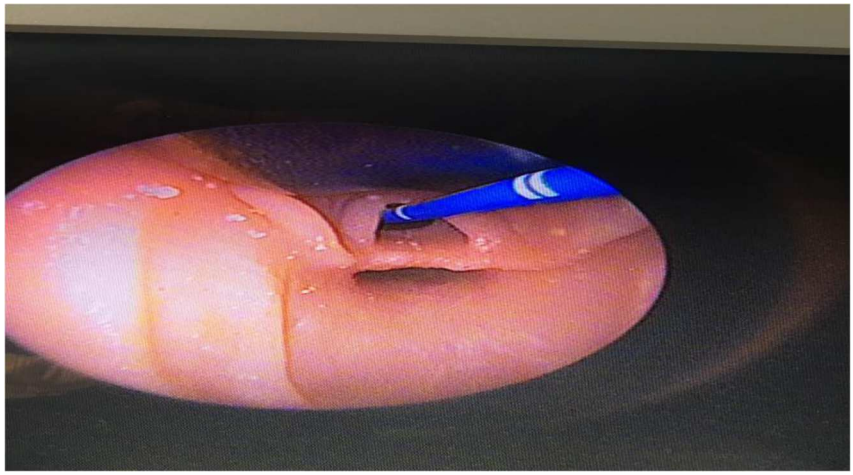
4.3.7 Procedure

It is essential that good neurodevelopmental care and effective non-invasive ventilation are maintained during the procedure.

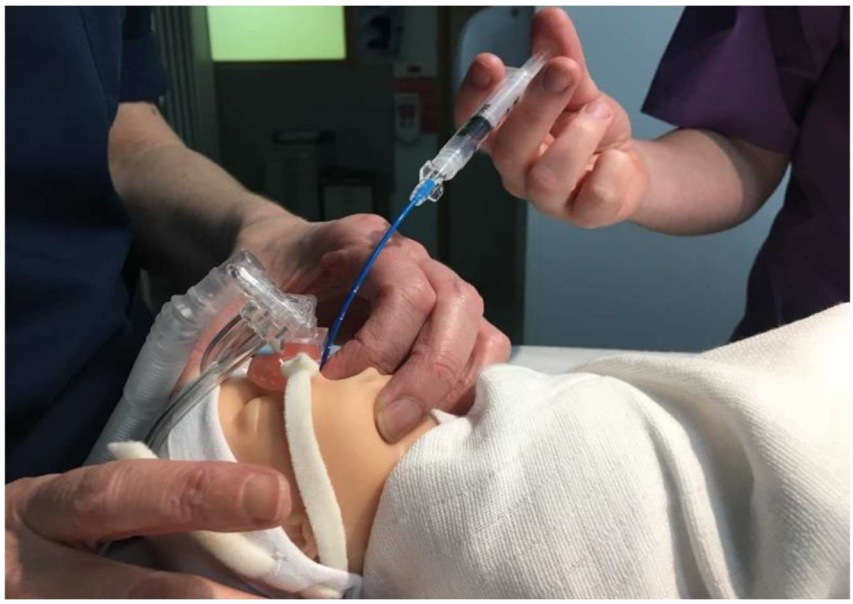
- Administer pre-medications, if appropriate, and wait for effect

- Insert laryngoscope to visualise cords - advance slowly to avoid stimulation of the posterior pharynx or larynx with the tip of the blade

- Pass catheter 1-2cm beyond cords depending on size of infant. Make a note of the length of the catheter at the lips. Avoid advancing the catheter too far as this may result in asymmetrical distribution of surfactant which can result in volutrauma and/or air leak



- **Remove the laryngoscope** and hold catheter against the edge of the mouth
- Keep mouth closed and maintain effective CPAP/HF



- Consider reversal of sedation e.g., naloxone if opiate sedation used
- Slowly administer surfactant over 2-3 mins while infant is spontaneously breathing
- Remove catheter and make sure infant is stable
- Consider aspirating NGT to demonstrate no surfactant in the stomach
- Complete local checklist/audit form as appropriate.

4.3.8 Anticipated Adverse Events

The most likely adverse event is hypoxia and/or bradycardia. This may occur during insertion of the laryngoscope or during administration of surfactant.

If there is hypoxia/bradycardia, pause and increase inspired oxygen. If no improvement, or the bradycardia is severe, administer intermittent positive pressure ventilation (IPPV). If there is persistent bradycardia induced by vagal stimulation, consider atropine at a dose of 10micrograms/kg.

If NIPPV is being provided using a ventilator, escalation of nasal prong pressures and inspiratory time can avoid swapping a nasal interface for a face mask device for IPPV.

In the event of prolonged deterioration or failure to respond to face mask IPPV proceed to routine intubation. In the face of persistent hypoxia consider the common causes of hypoxia in an intubated infant (DOPE) especially a pneumothorax.

4.3.9 Failure

If the sedation is ineffective, consider topping up with further sedation as per your unit's policy. If it is not possible to appropriately site the LISA catheter on the first attempt, it would be appropriate to attempt LISA a second time within the same procedure, if the first attempt fails.

If the procedure is unsuccessful or not tolerated, proceed to routine intubation, administration of surfactant and volume-guided ventilation. Aim to extubate as soon as it is appropriate and safe to do so.

4.4Supra-glottic airway devices (SADs) used for surfactant administration

A number of case series[vi] and RCTs[vii] have described a method of using supraglottic airway devices (SAD), such as iGels, to deliver surfactant in a specific group of patients with RDS to good effect. SADs are not appropriate for the more preterm or smallest neonatal patients e.g., <34 weeks and/or <1500g.

SAD insertion is thought to be less technically demanding than LISA using endotracheal passage of the catheter, and possibly easier in more vigorous, mature infants. Some units, especially LNUs who perform endotracheal intubation less frequently, see LISA via SAD as more likely to be successful due to the relative technical ease. The narrative review published by Roberts et al. [vii] describes a method of using SAD for LISA.

According to the most recent systematic review and meta-analysis of this topic, LISA via SAD[viii] results in reduced need for mechanical ventilation when compared to continued CPAP or INSURE. However, there is no comparison between LISA via SAD and via using a catheter and traditional laryngoscopy. The review also acknowledges that the only studies of surfactant administration via SAD are small and of varying methods, grading the quality of the evidence as very poor. Despite the possible benefits of LISA via SAD the review recommends that this method be confined to research studies only, therefore LISA via SAD should be considered experimental. It is not possible to recommend this method yet, until further research is obtained.

4.5 INSURE (INtubate SURfactant Extubate)

As detailed above, a recent Cochrane review found LISA was favourable when compared to INSURE. LISA is also the recommended method of surfactant administration in spontaneously breathing neonates with RDS in the European Consensus Guideline and should be the first line method of surfactant administration if appropriate and possible.

However, we recognise that INSURE is being practised in some units in the region where LISA is not yet routine care.

The indications and exclusions for INSURE would be the same as those detailed above.

The difference would be that the infant would receive a dose of fentanyl and a short acting muscle relaxant prior to endotracheal intubation. An experienced operator is needed to ensure success with one dose.

The patient would then receive bolus surfactant via the endotracheal tube followed by T-piece IPPV or volume-guided IPPV on the ventilator until the muscle-relaxant has worn off. Naloxone could be considered to minimise respiratory depression from the fentanyl. The patient would then be put back onto CPAP or HF once spontaneously breathing. It is very important to be cautious with inspiratory pressures during this method, as it is expected that the compliance of the lung will change in response to the surfactant. Therefore, extreme care must be taken to avoid barotrauma and volutrauma due to excessive pressures being used.

5. Audit Criteria

Completion of LISA checklist

6. Appendices

Appendix 1 Y&H ODN LISA Checklist

Appendix 1. Y&H Neonatal ODN LISA checklist

Name: Gestation: Birth weight:
ID Number: Date and Time of birth:

Decision making			
LISA guideline reviewed?	Y/N	Family aware?	Y/N
Indication ……..		Consultant discussed with ……..	
Difficult airway anticipated?	Y/N	Nurse in charge aware?	Y/N
Has pneumothorax been considered?	Y/N	Time decision to perform LISA ……..	

Equipment			
Video laryngoscope	☐	NG/OG in situ	☐
		Sedation drawn up (if appropriate)	
LISA catheter (consider extension)	☐	Drug…….. Dose……..	
		Intubation drugs prescribed and readily	
Sterile pack	☐	available	☐
Surfactant (200mg/kg to nearest vial)	☐	Intubation equipment readily available	☐
Labelled 5ml Luerlock syringe + needle	☐		

Preparation			
Patient positioned appropriately	☐	Monitoring attached	☐
Working IV access	☐	Plan for thermoregulation agreed	☐
Effective CPAP/HF in situ	☐	Procedure discussed and roles allocated	☐
Caffeine loading dose given	☐	Pre-oxygenate (saturations 90-95%)	☐
T-piece with pressures set	☐	Swaddled and sucrose given	☐

Say aloud "Is everyone ready? Quiet please!"

Procedure

Number of attempts (defined as laryngoscope passing lips) ……..
Desaturation <90%, duration and actions?
……..
Complications……..
Atropine required? Y/N Time surfactant given ……..
Observations post-procedure HR……SpO2……BP……Temp……..

Performed by: Name…….. Grade……..

Continuation notes:

Checklist completed by: Name……. Signature……
Grade…… Date and Time…….

7. Contributors and Sources

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8. References

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