


Surfactant Replacement Therapy for Neonates with Respiratory Distress

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Reference number	
Version	01
Author Name & Job Title	Dr Sankara Narayanan, Neonatal consultant, Watford
Executive Lead	East of England ODN
Contributors Names and Job Titles	None
Consultation	17 X Network hospitals & Clinical Oversight Group
Approved by speciality Date	
Date ratified	
Review date	
Target audience	Neonatal doctors, nurses, transport team
Additional Search Terms (Key Words)	Surfactant, RDS, Curosurf, Neonate, LISA, Intubation

Neonatal Clinical Oversight Group	Registration No:NEO-ODN-2018-14
Clinical Lead Mark Dyke	

Ratified December 2018

Review Date: December 2021

Change History

Version	Date	Author	Reason for change
			E.g. New Policy, Formal review, Informal review due to...
1		Dr S Narayanan	New network guideline

CONTENTS

1. Purpose of the Guideline:	4
2. Target Audience:	4
3. Introduction & Background:	4
4. Definitions:	4
5. Indications, preparation and dosage:	5
6. Surfactant administration procedure:	7
7. Adverse effects:	8
8. Post procedure care	8
9. Audit standards:	9
10. References	9

GLOSSARY OF TERMS

TERM	Gestation \geq 37 completed weeks
PRETERM	Gestation $<$ 37 completed weeks
Moderate/Late PRETERM	Gestation between 32 – 36 weeks
Very PRETERM	Gestation between 28 – 32 weeks
Extreme PRETERM	Gestation $<$ 28 weeks
RDS	Respiratory Distress Syndrome
NICU	Neonatal Intensive Care Unit
PH	Pulmonary Haemorrhage
INSURE	IN tubate, SUR factant and Ext ubate
LISA	L ess I nvasive S urfactant A dministration
MIST	M inimally I nvasive S urfactant T herapy

1. Purpose of the Guideline

To provide guidance on surfactant administration in preterm and term neonates who either present with, or are at high risk of developing, surfactant deficiency respiratory distress syndrome. The document outlines the indications, dosage, formulation and procedure for surfactant administration & timing/strategies for surfactant use. It also discusses the post procedure management; complications and sets out audit standards for monitoring compliance.

2. Target Audience

This guideline is intended for the use of neonatal medical and nursing staff in appropriate clinical areas (neonatal unit, delivery suite, maternity theatres and very rarely for a preterm neonate presenting to Children's Emergency Department following an out of hospital birth).

3. Introduction & Background

Respiratory distress syndrome (RDS) due to surfactant deficiency is a major cause of morbidity and mortality in preterm infants [1]. Secondary surfactant deficiency complicates other respiratory disorders in neonates such as meconium aspiration syndrome, sepsis/pneumonia, congenital lung malformations and possibly pulmonary haemorrhage.

There is good quality clinical evidence that links early surfactant treatment and reduced respiratory morbidity and improved survival without bronchopulmonary dysplasia [2, 3].

Natural surfactants are more beneficial when compared to synthetic surfactants in the treatment of respiratory distress syndrome. Babies (preterm and term) with respiratory distress where surfactant is indicated should receive a natural surfactant preparation [3]. Preparations available in the UK are:

Poractant alfa (Curosurf®, 120 mg / 1.5 mL & 240 mg / 3 mL, Chiesi Pharmaceuticals), a natural surfactant preparation of porcine origin

Beractant (Survanta® 200 mg / 8 mL, ABBVIE Ltd), a natural surfactant preparation of bovine origin

Definitions

a) Prophylactic surfactant therapy:

It is a preventative strategy where surfactant is routinely administered to preterm infants below a certain gestation threshold (usually < 28 weeks). This is usually done in delivery room soon after birth regardless of baby's condition or presence/severity of RDS. Surfactant should ideally be administered within 10 - 30 minutes of birth as per this strategy [1]. Though recent evidence does not support this treatment strategy [4], **babies who are likely to be transferred out to a NICU, it is pragmatic to intubate and administer surfactant and keep them ventilated pending transfer.**

b) Early rescue surfactant therapy:

Early rescue is defined as surfactant administration within 1 – 2 hours of birth for babies who show clinical symptoms/signs of RDS. This approach has been reported to be superior to prophylactic treatment in terms of reduction in mortality, air leak, chronic lung disease and/or death.

Early rescue treatment is considered as current standard [2,3]. Babies with RDS should be given surfactant early in the course of the disease. **A suggested protocol would treat < 26 week babies at FiO2 threshold**

of > 0.3 and > 26 week babies at $\text{FiO}_2 > 0.4$. However, surfactant should be administered as part of delivery room stabilisation (or soon after admission to neonatal unit) in preterm infants who need intubation as part of their stabilisation process or in a very preterm infant who is not steroid mature [2].

INSURE and LISA/MIST approaches should be considered. LISA may have marginal benefits when compared to INSURE. However, LISA technique requires specific equipment, training of healthcare professionals and consideration of modified sedation protocols. Detailed description of LISA/MIST is outside the scope of this guideline, units who are interested in implementing LISA/MIST are advised to develop their own guidelines about practical aspect of the procedure.

a. INSURE:

INTubate, **SUR**factant, **EXT**ubate is the recommended technique with a view to reducing baro/volutrauma and airway inflammation secondary to mechanical ventilation [5]. Consideration should be given towards continuing MV for infants that are being transferred to NICUs.

b. LISA/MIST:

Less invasive or Minimally Invasive surfactant administration/therapy has been developed in the recent years as an alternative to INSURE in avoiding intubation for surfactant delivery. This technique instead uses a thin catheter to deliver surfactant in a spontaneously breathing infant on nasal CPAP. A recent meta-analysis reported that LISA technique reduced the need for MV and reduction in composite outcome of BPD/death and BPD in survivors (4)

4. Indications, preparation and dosage:

- **Primary surfactant deficiency:**

- Preterm neonate 23 – 34 weeks with moderate to severe RDS and/or high risk of developing moderate/severe RDS (no or inadequate antenatal steroids, gestational diabetes etc.)

[Useful guide: Preterm babies with RDS on CPAP should be given surfactant if > 26 weeks and $\text{FiO}_2 > 0.3$ and > 26 weeks on $\text{FiO}_2 > 0.4$ **and/or** increased work of breathing with respiratory and/or mixed acidosis and/or radiographic evidence of neonatal RDS] [5]

- Late preterm infant/Early term infant with moderate to severe RDS requiring $\text{FiO}_2 > 0.4$ and/or increased work of breathing

- **Other indications in intubated infants (secondary surfactant deficiency):**

- Meconium aspiration syndrome
- Persistent pulmonary hypertension of newborn
- Congenital pneumonia
- Pulmonary haemorrhage (note this can be a rare complication of surfactant therapy in which case it should not be repeated)

- **Surfactant therapy not useful/not indicated:**

- Chronically ventilated preterm/term infants
- Congenital diaphragmatic hernia

- Infants ventilated for non-respiratory indications (e.g. neuromuscular problems, congenital anomalies etc.)
- Second dose of surfactant should be considered if there is on-going oxygen requirement (FiO₂ > 40%) and continuing need for mechanical ventilation. Second dose should preferably be not repeated within 12 hours of the first dose. However, some infants will need a repeat dose earlier, this should be discussed with consultant and reasoning clearly documented in notes. Occasionally, a third dose may be required.

- **Preparation & storage:**

- **Poractant alfa (Curosurf)**

- **Curosurf 120 mg®** / 1.5 ml vial Intratracheal Suspension
- **Curosurf 240 mg®** / 3 ml vial Intratracheal Suspension
- Stored in refrigerator (2 – 8° C, protected from light)



- **Beractant (Survanta)**

- 200 mg / 8 mL
- Stored in refrigerator (2-8 C, protected from light)



- **Dose**

○ **Curosurf**

- **200 mg/kg/dose** offers significant benefits than 100 mg/kg for treatment of surfactant deficiency RDS [5]
- **100 mg/kg/dose** for secondary surfactant deficiency or for repeat doses

○ **Survanta**

- **100 mg/kg**

5. Surfactant administration procedure:

(Additional info on surfactant administration available @ <https://youtu.be/noNN2ocs9ZY>)

- Clarify indication with consultant and agree on dose and strategy (INSURE, LISA/MIST or surfactant administration and ventilate)
- Prescribe on drug chart on the once only side. Round up to nearest multiple of 120 mg. E.g. Curosurf mg (.... mg/kg/dose) via endotracheal route. Document batch no(s).
- Prepare equipment:
 - Neo puff/Tom thumb (preferable) or neonatal self-inflating bag
 - Suction catheter and functioning suction apparatus,
 - Slowly warm up surfactant vial(s) to room temperature (placing in an incubator or within a closed fist for few minutes)
 - Turn the vial upside down a few times to ensure uniform suspension
 - Check colour (creamy white), expiry date and batch number
 - Pre-cut surfactant administration catheter (1-2 cm short of total endotracheal tube length including adapter),
 - 5 ml syringe X 2, (special syringe as surfactant coats normal syringes)
 - 18 G needle X 2
- Verbal consent from parents and document in notes, if possible [6]

Administration in delivery suite:

- Resuscitate/stabilise newborn as per first hour care and/or NLS guideline
- Intubate airway, confirm correct airway placement by ensuring bright yellow colour change on Pedi-cap
- Ensure adequate, symmetrical chest rise, stable heart rate > 100/min and saturations > 90 %
- Fix endotracheal tube at appropriate length at lips
- Ensure that baby is in supine position
- Draw up surfactant and rapidly administer using the administration set
- Withdraw syringe and draw up 1 ml of air and flush the surfactant catheter with air to ensure that surfactant has been administered
- Continue IPPV until heart rate and O₂ saturations are in satisfactory range
- Consider reducing PIP to decrease volutrauma following improved lung compliance after surfactant administration
- Transfer baby as soon as possible to neonatal unit after showing to parents
- Prescribe and sign prescription chart and document in clinical notes
- Complete high cost drug form (appendix A) & leave in nursing folder for consultant signature

Administration in neonatal unit:

- Draw appropriate dose of surfactant as prescribed
- Ensure proper endotracheal tube placement
- Suction ET tube if necessary
- Optimise ventilation/oxygenation as necessary
- Disconnect from ventilator and administer surfactant
- Connect to ventilator on targeted tidal volume or volume guarantee, alternatively hand ventilate gently on required pressures and reconnect to ventilator
- Once stable, reconnect to ventilator or extubate in case of INSURE
- Sign prescription chart and document procedure in clinical notes

6. Adverse effects

- Desaturations/bradycardia during/immediately after administration, usually resolves with IPPV
- Endotracheal tube blockage (if this results in desaturations/decrease in tidal volumes that doesn't improve with IPPV for 2-3 minutes, suction endotracheal tube to remove obstruction)
- Pulmonary haemorrhage

7. Post procedure care

- Remain by patient's cot side until you are satisfied that baby's clinical condition is stable
- Check oxygen saturations, tidal volume and ventilator graphics. Lung compliance rapidly improves and ventilator pressures may need to be reduced rapidly (if not on TTV) as guided by tidal volumes to prevent baro/volu-trauma
- Check a blood gas 15 – 30 minutes' post procedure
- Record any deterioration/adverse event or post procedure interventions in clinical records
- Suctioning should ideally be avoided for 1-hour post procedure, however, if surfactant is blocking the endotracheal tube and interfering with ventilation, prompt suctioning should be performed to clear obstruction
- Any unused, unopened but pre-warmed surfactant can be returned for storage in the refrigerator as long as it is within 24 hours- once only

8. Audit standards

- a) All preterm infants with RDS who need mechanical ventilation should be given a natural surfactant within 30 minutes of intubation.
- b) All preterm infants, in whom surfactant treatment is indicated, should receive an initial dose of 200 mg/kg (rounded up to the nearest multiple of 120 mg) of surfactant.
- c) All surfactant prescriptions should adhere to expected prescription standards as per Trust medicines management policy – Refer **Appendix B**

9. References

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