



Clinical Practice Guideline
Guideline coverage includes NICU KEMH, NICU PMH and NETS WA

Surfactant Therapy

This document should be read in conjunction with the [Disclaimer](#)

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Surfactant therapy is given to minimise atelectasis and reduce the work of breathing. This is achieved by reducing the surface tension and promoting alveolar stability during expiration.

Prophylactic surfactant administration is considered to be treatment in the delivery room before or shortly after the first breath. A single dose should be administered preferably within 15 minutes of birth.

Aim

This document covers two salient aspects of surfactant therapy in neonates.

- Indications for surfactant therapy in neonates.
- Type of surfactant: Poractant (Curosurf) or Beractant (Survanta).

Indications

- Ventilation for respiratory distress syndrome (RDS) and meconium aspiration syndrome (MAS).
- Consider in neonates with pulmonary haemorrhage.
- Consider with severe RSV bronchiolitis.

For all indications, it is preferable to use Survanta except in extremely preterm infants (≤ 25 weeks) where Curosurf is to be used.

Clinicians may choose to use Curosurf on an individual case basis if they consider that the baby's clinical condition warrants it.

Refer to the [Neonatal Medication Protocols](#) for details of the dose and method of administration of surfactant, [Survanta](#) / [Curosurf](#).

Further Reading

Key Points

- Medical Staff should be present during and for at least the first 5 minutes after administration to alter ventilation settings as required (ventilator rate, FiO_2 and inspiratory time settings). Any increase in ventilator settings should be based on the infant's tolerance of the procedure. Unnecessary increases may increase lung damage. Reassess ventilator settings every 15 minutes for an hour, then hourly thereafter. Note changes in SaO_2 , TV, MV.
- Curosurf can improve oxygenation and lung compliance more rapidly than Survanta. Increase in lung volume is an indication of improved lung compliance. Reduction in FiO_2 may be required within 5 minutes of administration.
- Adverse reactions to surfactant administration include transient hypoxia and bradycardia, oxygen desaturations, endotracheal tube blockage and air leaks. If there is significant desaturation or bradycardia, stop the administration temporarily.
- Surfactant administration is a two-person procedure. The infant must have cardio-respiratory monitoring throughout.

Administration Equipment and Procedure

Equipment

- Trachmac Device; size FG 5 for size 2, 2.5, 3, 3.5 endotracheal tubes.
- Surfactant (Survanta or Curosurf).
- 10 mL syringe, drawing up needle and alcohol wipe.

Administration

- Place the infant in the supine position. The base of the warmer or incubator is to remain flat throughout. Transcutaneous monitoring (TCM'S) advisable.
- Leave flow sensor in place (should be replaced after procedure if it becomes contaminated with surfactant).
- Remove the blue connector from the endotracheal tube and attach the appropriate adaptor and Trachmac device. Reconnect endotracheal tube to ventilator.
- Draw up the prescribed volume, add 1ml of air. Ensure that the air is at the plunger end of the syringe. Attach syringe to luer lock connector of Trachmac.



1. The **insertion distance** for the Trachmac is determined by the length of the ETT to the cut off point plus 5cms. (Note the colour band before the number for easier visualisation).
2. Insert the catheter & as soon as the colour appears in the “**window area**” of the Trachmac catheter - stop advancing the catheter (the tip will be at the end of the ETT to within 0.5 cm out of the end of the ETT).
3. Instil ½ of dose. Withdraw the trachmac catheter from the ETT and wait until vital signs are stable.
4. Instil 2nd aliquot of surfactant followed by air to clear surfactant from catheter.
5. Withdraw the trachmac catheter from the ETT as above.
6. Remove syringe and replace combi stop to connector.



- Alter ventilator settings as medically ordered.
- Take a blood gas at 15 - 30 minutes after administration to detect changes in lung function.
- Subsequent gases as ordered.
- Leave Trachmac device in situ for 2nd dose then discard.
- Change to Ballard suction device after second administration of surfactant is complete.
- Following administration, position prone if stable/practical.
- Complete documentation.

INTubate, SURfactant, Extubate (INSURE) Procedure

Further Reading

Indications

Note: INSURE method of administering surfactant is at the discretion of the on call consultant.

Any infants with clinical signs of respiratory distress or other evidence of RDS like abnormal gas (respiratory acidosis), Worsening FiO₂ requirement or abnormal CXR can be considered for the procedure.

- Eligible infants should have good respiratory effort
- Preferably less than 6 hours old (earlier the age of INSURE better the outcomes)

Infants that may not be good candidates for INSURE

- Intubated at birth for apnoeas/poor respiratory effort
- Neonates who have received extensive resuscitation
- Any associated medical issues e.g. Anaemia, Hydrops

Procedure

- **No premedication.**
- [Intubation](#) as per Neonatal Clinical Guidelines.
- Tube size according to the gestational age and weight or a smaller sized ETT.
- Check tube placement with CO₂ indicator, and auscultation.
- Curosurf/ Survanta to be administered in 2 bolus aliquots as per [Surfactant Administration](#) Procedure above.
- Ventilate with manual breaths via Neopuff following surfactant administration with prolonged inspiratory time.
- The patient is then to be extubated to nCPAP.

Before Extubation ensure

- HR & saturations are stable.
- FiO₂ less than the pre-surfactant level.
- No apnoeas.

Other recommendations

- One-to-one nursing is recommended for the duration of the administration and observations.
- Senior Registrar or Consultant to supervise administration of appropriate dose of surfactant.
- Ventilate using the Neopuff until stable.
- If transient bradycardia or desaturation present, briefly stop the dosing procedure and initiate Neopuff.
- Once the infant has stabilized, resume the dosing procedure.
- Keep ventilator as a standby.
- Extubate to CPAP as soon as possible.
- If possible Registrar/SR to remain on NICU for 30 minutes following Extubation.
- Blood gas 30 minutes- an hour after procedure.

Surfactant therapy in neonates (Further Reading)

Summary: Surfactant needs to be administered to neonates ventilated for hyaline membrane disease (HMD) and meconium aspiration syndrome. Surfactant therapy may be considered in neonates with pulmonary haemorrhage and severe RSV bronchiolitis. There is no evidence to support the use of Surfactant therapy in congenital diaphragmatic hernia. For all indications, it is preferable to use Survanta except in extremely preterm infants (≤ 25 weeks) where Curosurf is to be used. Clinicians may choose to use Curosurf on an individual case basis if they consider that the baby's clinical condition warrants it. Please refer to the NICU drug manual for details of the dose and method of administration of surfactant .

Indications for surfactant therapy in neonates:

Hyaline Membrane Disease: Multiple RCTs have shown that animal derived surfactants, either given prophylactically in the delivery room or as rescue therapy are known to improve the outcomes of preterm infants with HMD (Singh 2015). The attending neonatologist or the senior registrar will decide regarding whether to use administer it prophylactically in the delivery room or later in the NICU.

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Surfactant administration in non-HMD conditions in neonates:

Surfactant administration in non-HMD conditions have been covered by the two recent and excellent reviews: One from Bonny Jasani et al (2016) and the other from Keiser et al (2016) from the USA.

Pulmonary haemorrhage: While there are few small observational studies that have shown beneficial effects of surfactant administration in pulmonary haemorrhage, there are no RCTs that have examined this issue. The review articles by Keiser (2016) and Jasani (2016) came to similar conclusions that there remains insufficient evidence to recommend the routine use of surfactant after pulmonary haemorrhage in preterm infants.

In an RCT, Bozdaq et al (2015) compared poractant alfa ($n=21$) and beractant ($n=21$) for the treatment of pulmonary haemorrhage in very low birth weight infants. In both the groups, the mean standard deviation (SD) birth-weight and gestational age were similar ($p = 0.33$ and 0.89 , respectively). There was no significant difference between the groups for OI values at all-time points ($p > 0.05$). The rates of Broncho pulmonary dysplasia (BPD) and mortality related to pulmonary haemorrhage were similar in both the groups. They concluded that both natural surfactants improved oxygenation when administered for pulmonary haemorrhage in VLBW infants. They also concluded that the type of surfactant seems to have no effect on BPD and mortality rates in these patients.

Meconium aspiration syndrome: The Cochrane review (El Shahed A 2014) included four randomised controlled trials met inclusion criteria. Three out of those four trials used Beractant, whereas one used Poractant. The meta-analysis of four

trials (326 infants) showed no statistically significant effect on mortality [(RR) 0.98, 95% confidence interval (CI) 0.41 to 2.39]. The risk of requiring extracorporeal membrane oxygenation was significantly reduced in a meta-analysis of two trials (n = 208); [RR 0.64, 95% CI 0.46 to 0.91]. Both trials used Beractant.

Congenital diaphragmatic hernia: Keiser et al (2016) concluded that on the basis of review of the literature, there remains insufficient evidence to recommend the routine use of surfactant in the management of term infants with CDH, regardless of need for ECMO support. This includes the subpopulation of preterm infants with CDH. Similar conclusions were drawn by Jasani et al (2016).

Critically ill infants with RSV Bronchiolitis: Jat et al (2015) evaluated the role of surfactant administration in critically ill infants with RSV Bronchiolitis. They identified only three RCTS (Total sample size 79) and found that the use of surfactant had favourable effects on duration of mechanical ventilation, duration of ICU stay, oxygenation, and CO₂ elimination. Two of the included trials used Curosurf whereas the other trial used Survanta.

Poractant versus Beractant in preterm infants with hyaline membrane disease:

The Cochrane review (Singh et al, December 2015) identified nine studies that compared modified bovine minced lung surfactant extract (Beractant/Survanta) to porcine minced lung surfactant extract (Poractant/Curosurf). Meta-analysis of these trials demonstrated a significant increase in the risk of worse outcomes for Beractant: Mortality prior to hospital discharge (RR 1.44, 95% CI 1.04 to 2.00; 9 studies and 901 infants; moderate quality evidence), death or oxygen requirement at 36 weeks' postmenstrual age (RR 1.30, 95% CI 1.04 to 1.64; 3 studies and 448 infants; moderate quality evidence), and patent ductus arteriosus (PDA) requiring treatment (RR 1.86, 95% CI 1.28 to 2.70; 3 studies and 137 infants).

While at the outset it appears that Curosurf is superior to Survanta, it is important to note that the total sample size was only 901 infants from 9 RCTs. In the same Cochrane review, under the title 'implications for practice', the authors stated that 'caution should be used in the interpretation of this result because of the imprecision in analysis from the small sample size of the studies'. They also stated that "due to the lack of information about long-term neurodevelopment, respiratory and other health effects, no conclusions can be drawn about the superiority or inferiority of one animal-derived surfactant over another with respect to long-term outcomes".

The European consensus guidelines recommend the use of Poractant for HMD in preterm infants (Sweet DG, 2013). Poractant Alfa in an initial dose of 200 mg/kg is better than Beractant for rescue therapy. The American Academy of Pediatrics (Polin R, 2014) does not make such recommendations. They say it is unclear whether significant differences in clinical outcomes exist among the available animal-derived products.

We published a retrospective cohort study comparing the outcomes of inborn preterm infants <32 weeks gestation (23-31(+6) between 2005 and 2007. 415 preterm infants (<32 weeks) received surfactant (Curosurf: 214; Survanta: 201) (Paul, 2013). Infants in the Curosurf group were 2.8 days younger than Survanta

(27.0 ± 2.3 vs. 27.4 ± 2.3 weeks; $P = 0.03$). All other baseline characters including Clinical Risk Index for Babies II scores were similar for both groups. No significant differences between Curosurf and Survanta were found for the following outcomes: death or chronic lung disease (78/212 vs. 59/200; $P = 0.28$); death (24/214 vs. 15/201, $P = 0.24$); moderate to severe chronic lung disease (63/212 vs. 46/200; $P = 0.45$) and moderate to severe disability (20/163 vs. 19/151, $P = 0.98$). Subgroup analysis of infants <28 weeks and ≥ 28 weeks also did not show significant differences between the two types of surfactant. Subgroup analysis of infants <25 weeks showed that Survanta group had higher incidence of the composite outcome of death or CLD (31/40 vs 26/27). Infants >25 weeks who received Curosurf had higher incidence of 'death or CLD' (47/172, 27.3% vs 33/173, 19.3%, $p=0.023$) (Paul et al, PAS abstract 2012). The results remained the same even on multivariate logistic regression analysis. We concluded that the results of our study do not support the need for preferential use of Curosurf or Survanta.

Cost of Curosurf versus Survanta for the NCCU of KEMH/PMH:

For our unit, the cost of a 3-mL vial (240 mg surfactant) of Curosurf is AUD 819.00, whereas the cost of 8 mL (200 mg surfactant) Survanta is AUD 346.35. For a baby with birth weight of 1000 g, the cost of Curosurf using the standard regimen of initial 200 mg/kg (2.5 mL/kg) followed by 100 mg/kg (1.25 mL/kg) is \$1023.00. For a baby with same birth weight, the cost of Survanta using the standard regime of initial dose of 100 mg/kg (4 mL/kg) and subsequent dose of 100 mg/kg (4 mL/kg) is \$346.35. This represents 2.95 times higher cost for Curosurf over Survanta. Even if one were to use the INSURE technique (intubation, surfactant and extubation) with Curosurf and use only one dose, the cost will be AUD 682.00, which is 1.97 times more expensive than two dose regimen of Survanta. Given that Curosurf is very expensive and there is lack of strong evidence of benefit, it is preferable to use Survanta in the NCCU for all indications except in extremely preterm infants (≤ 25 weeks) where Curosurf is to be used. Clinicians may choose to use Curosurf on an individual case basis if they consider that the baby's clinical condition warrants it.

INSURE Method (Further Reading)

Background

Respiratory Distress Syndrome is the most important cause of mortality and morbidity in preterm infants. More than 60 years after the discovery of surfactant, still there is no optimal approach to the respiratory management (Editorial Clin Perinatology 39, 2012). Introduction of CPAP more than halved the mortality from 55 to 20% and surfactant treatment has halved the mortality from 20 to 10%.

Evidence from systematic review showed that Early surfactant treatment reduces mortality and decreases the incidence of chronic lung disease (CLD) and air leaks in preterm infants at risk of RDS (Yost CC, Soll RF Cochrane Database Syst Rev 2000). Multiple reviews since then have shown the benefit of early surfactant use.

One of the major drawbacks of conventional way of surfactant administration is the complications and adverse effects associated with this procedure. Evidence from animal research showed that mechanical ventilation triggers inflammatory lung injury & decreased incidence in CPAP (Jobs AH 2002) & best approach would be avoidance of mechanical ventilation (Avery ME 1987, Polin RA 2002). Other long

term complications include subglottic stenosis/ cyst formation (Johnson LB 2005), and voice changes (French N, 2013).

Why INSURE?

Respiratory support through non-invasive approach is increasingly being achieved through nasal continuous positive airway pressure (CPAP). Nasal CPAP is associated with a decreased risk of developing chronic lung disease compared with conventional mechanical ventilation.

An INtubate, SURfactant, and Extubation (INSURE) strategy has been successfully applied both early and late in the course of respiratory distress syndrome. While we are waiting for more evidence for administering exogenous surfactant through non-invasive approaches this INSURE seems to be the most reasonable method of administering surfactant in the eligible and suitable group of infants (Pfister, & Soll, Clin Perinatol 39, 2012).

Current Evidence for INSURE

The INSURE method has been reported in several different contexts and compared with existing respiratory support strategies. Both early INSURE (during initial hour of life) and late INSURE (used later in the course of established RDS) strategies have been compared with the conventional standard approach of intubation, surfactant administration and continued mechanical ventilation and compared with continued nasal CPAP.

INSURE method seems to reliably reduce the burden of mechanical ventilation in preterm infants with RDS with early INSURE being more beneficial. Some infants still fail, requiring re-intubation and mechanical ventilation (30-50%) (Pfister, & Soll, Clin Perinatol 39, 2012).

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Related WNHS policies, procedures and guidelines

Neonatal Clinical Guidelines - [Intubation](#)

[Neonatal Medication Protocols](#)

Neonatal Medication Protocols - [Survanta](#)

Neonatal Medication Protocols - [Curosurf](#)

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