

Respiratory failure secondary to surfactant deficiency is a major cause of morbidity and mortality in preterm neonates. Exogenous surfactant therapy substantially reduces mortality and respiratory morbidity.

Type of surfactants

Table 55.1 enlists the different types of surfactant commonly used in NICUs.

Table 55.1: Commonly used surfactant preparations

Natural	Minced lung extracts	1. Beractant (Survanta) 2. Poractant alfa (Curosurf) 3. Surfactant TA (Surfacten)
	Lung lavage extracts	1. Bovine Lipid Extract Surfactant (BLES) 2. Calfactant (Infasurf) 3. SF-RI1 (Alveofact)
Newer synthetic	New synthetic (protein analogues); second generation	1. Lucinactant (Surfaxin)-SPB analogues, Sinapultide 2. rSP-C surfactant(Venticute)-SPC analogues, Lusupultide
	Third generation synthetic	CHF 5633 (SP-B and SP-C enriched synthetic surfactant)

Note :

1. Minced lung extracts contain less than 10% of the SP-B that is found in the lung lavage extracts.
2. Synthetic surfactants do not have the theoretical concerns associated with animal-derived surfactants like transmission of microorganisms, exposure to animal proteins and inflammatory mediators, susceptibility to inactivation, and inconsistent content.
3. First generation protein free synthetic surfactants are not used nowadays.

Dosage

Term neonates usually have a surfactant storage pool of approximately 100 mg/kg, whereas preterm neonates have an estimated pool only 4–5 mg/kg at birth. Exogenous surfactant therapy increases the pool size rapidly and improves pulmonary gas exchange until endogenous surfactant is

released. So a minimum of 100 mg/kg of surfactant should be administered to preterm neonates with RDS. Higher dose of poractant (200 mg/kg) has been shown to be superior in reducing mortality and BPD as compared to low dose poractant or beractant.

Table 55.2: Common brands of surfactant and their dosage

Surfactant preparations	Survanta (Abbvie)	Curosurf (Nicholas)	Neosurf (Cipla)
Dose (Phospholipids)	4 mL/kg (100 mg/kg)	2.5 mL/kg (200 mg/kg)	5 mL/kg (135 mg/kg)
Available formulation	4 mL and 8 mL	1.5 mL and 3 mL	3 mL and 5 mL
Cost (₹)	8800 and 14500	11780 and 20790	4900 and 7950

Indications for surfactant therapy

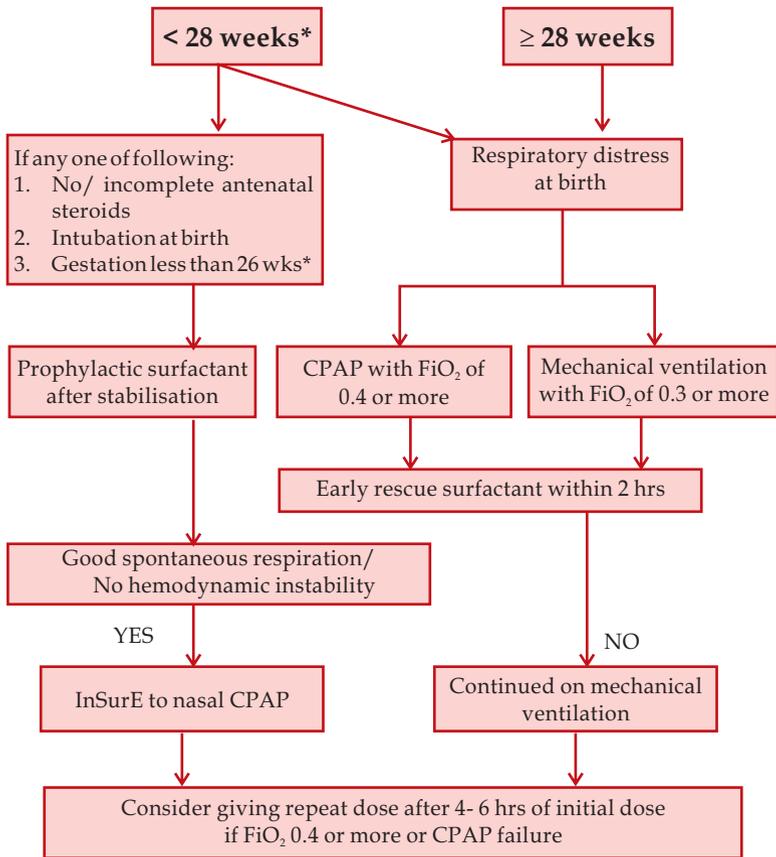
Surfactant replacement is done mainly for RDS. But it can be used in other conditions where surfactant is inactivated such as meconium aspiration syndrome, pneumonia, pulmonary hemorrhage, congenital diaphragmatic hernia and acute respiratory distress syndrome.

In RDS, surfactant can be administered either prophylactically or as rescue therapy.

1. **Prophylactic surfactant:** Surfactant is administered within 15- 30 min of birth, irrespective of the presence of symptoms of RDS. Prophylactic SRT is given in preterm neonates <28 weeks of gestation, if no or incomplete antenatal steroids to mother or if requiring intubation and mechanical ventilation at birth.¹⁻³

Rationale: Administration of surfactant to a previously unventilated or minimally ventilated lung will diminish acute lung injury. Acute lung injury results in alveolar-capillary damage, leakage of proteinaceous fluid into the alveolar space and release of inflammatory mediators, resulting in decreased response to surfactant replacement.

2. **Early rescue:** Surfactant is administered in preterm neonates with RDS within 2 hours of birth. Early administration of surfactant is advantageous as the presence of lung fluid helps in uniform distribution of the



*Individualised decision to be taken for giving prophylactic surfactant in this age group

Figure 55.1: Surfactant replacement therapy in neonate

surfactant. It also ensures that surfactant is administered before widespread atelectasis develops in the lungs. Early rescue surfactant therapy following a trial of CPAP is preferred over prophylactic therapy because the immediate outcomes are comparable and the amount of surfactant used is reduced.

- Late rescue:** Surfactant is administered after 2 hours. It is done usually in outborn neonates who are transported late to referral centers.

Procedure for surfactant administration

Standard method of surfactant administration is through the endotracheal tube after intubation (Table 55.3).

Table 55.3: Procedure for surfactant administration

1. A physician or a nurse experienced in surfactant administration should administer the surfactant.
2. Warm the surfactant prior to administration (for at least 8 minutes if the vial is held between the palms of the hands or for 20 minutes at room temperature.) The vial should not be heated and it should not be kept on radiant warmer. It should not be kept in room air for more than 30 min as it increases viscosity.
3. Do not shake the surfactant.
4. Intubate the baby with appropriate size endotracheal tube.
5. Assess breath sounds for equality. Chest x ray is not mandatory for confirmation of ET tube position.
6. The neonate should be connected to a pulse oximeter and oxygen saturation and heart rate have to be monitored throughout the procedure.
7. Administer the surfactant through the feeding tube inserted in the ET tube or through the side port of the ET tube (if available)
8. Surfactant is given as bolus instillation in four aliquots of the total dose. No position change is required between the aliquots.
9. Connect the neonate to ventilator or the resuscitation bag or T piece resuscitator with set PIP and PEEP and ventilate carefully till saturation and heart rate stabilizes before administering next aliquot.
10. Increase PIP by 10 % for at least 5 min after surfactant administration and frequency of 60 breaths/min for uniform distribution
11. Suctioning of ET tube should be avoided at least 2 hrs following surfactant administration

*Strict asepsis should be carried out throughout the procedure

Methods of surfactant administration

Surfactant preparations must spread uniformly throughout the lung into the air-liquid interface once instilled in the proximal airways.

1. **Slow infusion versus rapid bolus administration-** Surfactant can be administered either by slow tracheal infusion or rapid bolus administration. Natural surfactant works best if given by a rapid bolus into the lungs as it leads to homogeneous distribution of surfactant and also results in rapid improvement in oxygenation. But it can also cause obstruction of the ET tube, transient bradycardia, hypotension and changes in cerebral blood flow. Currently,

rapid bolus technique is the recommended method of surfactant administration.

2. **Less invasive surfactant administration (LISA)** - Because of the risk associated with ET tube placement and ventilation, newer techniques with less invasive therapy have emerged. Surfactant is administered through a feeding tube (4-5 Fr catheter) inserted into trachea using Magill forceps under direct laryngoscopy without intubation. During this technique, CPAP is continued to facilitate alveolar recruitment which helps in the distribution of surfactant and avoids positive pressure ventilation.
3. **Minimally invasive surfactant therapy (MIST)** - Surfactant is delivered using a slightly stiff catheter like angiocath 16 G without using Magill forceps.
4. **Through laryngeal mask airway**- Trials used LMA for surfactant therapy in neonates of more than 1000 g showed that there is less need for mechanical ventilation. Surfactant reflux and coughing is more frequently seen with this method.
5. **Nebulised surfactant delivery**- It is truly non invasive technique. Practical issues like loss of surfactant in upper airway/esophagus, inactivation of surfactant and nonhomogenous distribution need to be addressed before this method can be recommended.

InSurE

InSurE stands for Intubate – Surfactant – Extubate to CPAP. InSurE comprises of intubation, surfactant administration, brief period of ventilation (usually < 1 hour) and rapid extubation to nasal CPAP to prevent ventilation induced lung injury (VILI). In neonates with signs and symptoms of RDS, InSurE to nasal CPAP results in decreased duration of mechanical ventilation, air leak and less incidence of BPD. InSurE technique may not be successful in the presence of severe birth asphyxia, lack of complete course of antenatal steroids, extreme prematurity, delayed administration of surfactant and shock.

Repeat dose of surfactant

Multiple doses had a stronger effect than single doses. Repeat doses of surfactant may be required if the administered

surfactant is inhibited by edema fluid, soluble proteins and inflammatory mediators which are present in the alveoli after lung injury due to mechanical ventilation and in neonates with delayed surfactant administration or sepsis, lower gestation/ birth weight and male sex. Neonates may require repeat doses of surfactant if they require FiO_2 0.4 or more on CPAP and mechanical ventilation to maintain a target saturation. Administering more than three doses has not been shown to have a benefit.

Poor response to surfactant

Some neonates may not show expected response to surfactant administered (RDS plus). These non responders either have lung injury prior to birth (infection), lung injury after birth and prior to treatment (large tidal volume), asphyxia, sepsis/pneumonia, meconium aspiration, severe disease, pulmonary hypoplasia, or concomitant cardiovascular (low blood pressure, congenital heart disease) conditions.

Adverse reactions of surfactant administration

Surfactant replacement therapy is much safer and side effects are usually transient. Hypoxia and bradycardia can occur during surfactant instillation due to acute airway obstruction. Other less common acute adverse effects include reflux of surfactant into the pharynx, increase in PCO_2 , gagging and mucous plugging of ET tube. There is an increase in the risk of pulmonary hemorrhage following surfactant therapy which is more common with natural surfactants (5% to 6%) than with synthetic surfactants (1% to 3%). Pulmonary hemorrhage typically occurs within 72 hrs and is due to improvement in lung compliance after surfactant therapy which promotes an increase in left-to-right shunt through the PDA resulting in increased pulmonary blood flow and pulmonary congestion.

Surfactant replacement therapy: what is the evidence?³⁻¹⁰

Prophylactic versus selective surfactant

Studies conducted prior to the routine application of CPAP demonstrated a decrease in the risk of air leak and neonatal mortality associated with prophylactic administration of surfactant. However, when all studies were

evaluated together, no benefits of prophylactic surfactant could be demonstrated and there is higher incidence of BPD or death in prophylactic surfactant group (RR-1.13; 95% CI 1.02–1.25) (Cochrane 2012).

Early rescue versus late rescue surfactant

Early rescue surfactant reduces the risk of neonatal mortality (RR 0.84; 95% CI 0.74 to 0.95), CLD (RR 0.69; 95% CI 0.55 to 0.86) and overall air leak syndromes (RR 0.61; 95% CI 0.48 to 0.78) (Cochrane 2012).

InSurE

InSurE compared with surfactant administration followed by continued mechanical ventilation and extubation from low respiratory support was associated with a lower incidence of need for mechanical ventilation [RR 0.67, 95% CI 0.57, 0.79], air leak syndromes [RR 0.52, 95% CI 0.28, 0.96] and BPD [RR 0.51, 95% CI 0.26, 0.99] (Cochrane 2007).

SRT in LMIC

Systematic review on SRT in preterm neonates with RDS from LMICs showed a significant reduction in mortality (RR 0.67; 95% CI 0.57 to 0.79) and air leaks (RR 0.51; 95% CI 0.29 to 0.90).

Long term outcome

No significant differences have been reported in the long-term neurodevelopmental outcomes and improved or to have equivalent results on pulmonary function testing in infants treated with surfactant compared to those treated with placebo.

New synthetic versus animal derived surfactant

Protein containing synthetic surfactant compared with animal derived surfactant didn't demonstrate any significant reduction in risk of mortality (RR 0.81, 95% CI 0.64- 1.03) or BPD (RR 0.99; 95% CI 0.84- 1.18).

Single dose versus multiple doses of surfactant

Repeat dose of surfactant administration results in lower incidence of pneumothorax (RR 0.51, 95% CI 0.30 - 0.88) and a decreased trend towards mortality (RR 0.63, 95% CI 0.39, 1.02).

Less invasive surfactant administration (LISA)

Meta-analysis of 6 trials compared LISA technique with intubation for surfactant delivery resulted in reduced composite outcome of death or BPD at 36 weeks (RR 0.75; 95% CI 0.59 to 0.94), BPD at 36 weeks (RR 0.72; 95% CI 0.53 to 0.97) or need for mechanical ventilation anytime during NICU stay (RR 0.66; 95% CI 0.47 to 0.93).

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