Surfactant in Preterm Infants

Introduction

Pulmonary surfactant is a complex mixture of phospholipids and proteins that serves to reduce alveolar surface tension. It is formed by type II pneumocytes from about 20 weeks of gestation. Surfactant creates a continuously reforming surface layer over the alveoli which reduces surface tension, prevents atelectasis and maintains alveolar stability. A deficiency or dysfunction in pulmonary surfactant production causes Respiratory Distress Syndrome (RDS). Risk factors associated with RDS are shown in Table 1, and incidence of RDS at RPA 1992-8 in Figure 1.

Exogenous surfactant has been shown to reduce neonatal mortality, death or bronchopulmonary dysplasia (BPD) and airleaks. The principle of administration is to deliver surfactant as early as possible to those infants with a high probability of surfactant deficiency.

<table>
<thead>
<tr>
<th>Increase RDS risk</th>
<th>Decrease RDS risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreasing gestational age</td>
<td>Antenatal steroids</td>
</tr>
<tr>
<td>Decreasing birth weight</td>
<td>Spontaneous labour</td>
</tr>
<tr>
<td>Male sex</td>
<td>Delivery after 38 weeks</td>
</tr>
<tr>
<td>Advanced maternal age</td>
<td>Histological chorioamnionitis</td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td></td>
</tr>
<tr>
<td>Elective and emergency caesarean section</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Factors affecting the development of RDS

![Incidence of RDS and surfactant requirement in RPA Newborn Care 1992-8](image)

**Figure 1.** Incidence of RDS and surfactant requirement at RPA Newborn Care, 1992-1998
Evidence for Surfactant in Preterm Infants

The following summarises the evidence for exogenous surfactant in preterm infants.

Natural versus synthetic surfactant

Both natural and synthetic surfactants are effective in the treatment and prevention of RDS. They reduce the risk of airleak, BPD and neonatal mortality\(^1-2\). Natural surfactant is associated with greater early improvement in the need for ventilatory support, fewer pneumothoraces and fewer deaths\(^7\).

Dose of surfactant

3 RCTs have shown that 200 mg/kg of poractant compared to 100 mg/kg of poractant or 100 mg/kg beractant significantly reduces neonatal mortality, with a NNT of 13 to prevent one death comparing 200 mg poractant to 100 mg/kg poractant\(^8-10\). The reduction in mortality was seen predominantly in those less than 32 weeks gestation. There was also a reduced need for subsequent doses of surfactant; from 59% in the 100 mg/kg group to 36% in the 200 mg/kg group\(^9\).

Early versus delayed selective surfactant treatment

The Cochrane review comparing early surfactant treatment of infants with signs of RDS to later selective treatment shows a reduced risk of airleak, neonatal mortality and chronic lung disease\(^11\). The major concern surrounding the early use of surfactant is the unnecessary intubation of infants who do not require it. For example, Gortner and colleagues\(^12\) studied 317 infants between 27-32 weeks, comparing early surfactant treatment of any infant that required intubation to later selective treatment of infants with signs of RDS. In each group one third of infants did not require intubation, and in the later selective group 58% of patients did not require surfactant.

Judging which infants are most at risk of RDS continues to be difficult. There is insufficient evidence to determine an accurate threshold for early surfactant administration. A trial in infants on CPAP of lower threshold for intubation with rapid extubation versus a higher threshold (a/A ratio <0.35 versus <0.22, approximately equivalent to a FiO\(_2\) of 0.37 versus 0.55) found a significantly reduced rate of death or need for mechanical ventilation in the first 7 days\(^13\).

Prophylactic (delivery room) versus selective surfactant

Prophylactic surfactant administration to infants at risk of RDS (<30-32 weeks) decreased the incidence of airleak and neonatal mortality when compared to giving later surfactant to those developing signs of RDS\(^14\). However, there are a number of problems in interpreting the trials included in this meta-analysis, with the rescue arms having high thresholds for surfactant treatment and considerable delays in time to treatment. Between 19-68% of infants in the control arms never required intubation and there was a low rate of antenatal steroid usage (4-48%). Given the current high rates of steroids in use at RPA (>90%), the number of infants who receive unnecessary intubation and surfactant is likely to be even higher.

If one considers subgroup analyses of the trials by Kendig\(^15\) and Egberts\(^16\), the majority of the reduction in mortality was seen in infants less than 26 and 27 weeks respectively. Therefore it is reasonable to consider a lower gestational threshold for prophylactic surfactant administration.

A trial of preterm infants (<29 weeks) randomised to immediate bolus (before ventilation) versus post-ventilatory surfactant (after resuscitation but before 15 minutes of age) showed no difference in mortality at discharge\(^17\). It is our preference that infants be adequately stabilised in the delivery room prior to surfactant administration.

Retreatment

Multiple doses of natural surfactant results in greater improvements in oxygenation and ventilatory requirements, a decreased risk of pneumothorax, and a trend towards improved survival\(^18\). However, there is limited evidence to suggest what criteria we
should use for giving further doses of surfactant. Kattwinkel et al. studied 1267 infants comparing a strategy of giving a further dose of surfactant at a low (0.3) versus a high (0.4 and a MAP of 7 cm H2O) oxygen threshold. There was no benefit in treating uncomplicated infants at a lower threshold, but complicated infants (evidence of sepsis or perinatal compromise) had a lower mortality when treated at the lower threshold.

**Early surfactant with brief ventilation versus selective surfactant with continued mechanical ventilation (In-out surfactant)**

The Cochrane review of 6 trials studying infants with signs of RDS compared early surfactant with less than 1 hour of ventilation to later, selective surfactant followed by continued mechanical ventilation and extubation from low ventilatory support. It showed less need for mechanical ventilation and a lower incidence of BPD and airleak syndromes in those given 'in-out' surfactant. There are a number of problems in interpreting this data. These trials were again done in an era of decreased antenatal steroid use (between 43-93%, with only one trial having more than 62% coverage), making this less comparable to our population. The studies not only compared surfactant and early extubation, but by design early versus late surfactant, complicating the specific question asked of these trials. The subsequent ventilation criteria for administration of surfactant varied between trials, but would be considered to be high by current standards. Although there were no reported complications of intubation and surfactant administration, another major cost of this approach is exposing infants unnecessarily to intubation and ventilation, even if for a short period of time. Between 30-57% of patients in the control groups never required surfactant, particularly the more mature and larger infants. The trials predominantly included infants more than 28 weeks of gestation, and this approach has not been adequately studied in the extremely preterm infant. At present therefore, the preference at RPA is to aim to extubate infants as early as possible from mechanical ventilation when the ventilatory support is minimal without excessive work of breathing and the infant has regular respiratory effort.

**Guidelines for Exogenous Surfactant Treatment in RPA Newborn Care**

**Less than 27 weeks**

Intubate in the delivery room and provide surfactant as soon as the infant has been stabilised unless the infant is low risk due to presentation (eg PPROM) or very vigorous with minimal respiratory distress.

**27-32 weeks**

If there is a requirement for intubation in the delivery room, administer surfactant after intubation and resuscitation. For infants not intubated in the delivery room, surfactant should be given if intubation and ventilation is provided at any time. Surfactant should be provided if an infant has respiratory distress despite adequate CPAP and requires FiO2 >0.35. However, a lower threshold should be considered in more immature babies, those with moderate or severe respiratory distress, or rising oxygen requirement in the first few hours of life.

**32-37 weeks**

Ventilated infants >32 weeks should receive surfactant unless the click test is positive, or is on minimal respiratory support with the view to extubation and a normal CXR. If the infant has respiratory distress on CPAP, the infant should be intubated and surfactant given if the FiO2 is >0.35 in the first 24 hours, or >0.4 subsequent to that. Lower thresholds should be considered in more immature babies, those with moderate or severe respiratory distress, or rising oxygen requirements in the first few hours of life.

These guidelines are summarised in Figure 2.

If there is sufficient expertise available, the click test should be performed in intubated infants prior to surfactant administration, particularly in more mature infants or if the diagnosis of RDS is in doubt. This results in earlier and reduced use of surfactant than standard rescue therapy using clinical and x-ray criteria for surfactant. The performance of a CXR should not delay the
administration of surfactant.

Surfactant should be given as early as possible i.e. before vascular access, unless required for resuscitation. Extubation after surfactant should be considered as soon as the infant is clinically stable on minimal ventilatory requirements and with adequate respiratory drive.

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**Dose**

The surfactant of choice in the RPA Newborn Care is poractant alfa (Curosurf, Chiesi Pharmaceuticals).

**Less than 32 weeks**

The dose is 200 mg/kg for the first dose of surfactant in infants less than 32 weeks. Subsequent doses are 100mg/kg.

**32 weeks and above**

First and subsequent doses in infants 32 weeks and above are 100 mg/kg.

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**Procedure:**

**Ensure correct endotracheal tube placement**

Confirm this clinically by seeing the endotracheal tube pass through the cords by 2cm, with a CO2 detector, auscultation of both lung fields, and clinical improvement (increase in heart rate and saturations) after intubation. Document the distance at the cords and at the nose or mouth and crosscheck with the chart of ETT lengths.

**Method**

Using aseptic technique, draw up the Curosurf. Cut a 5 Fr feeding catheter to the length of the endotracheal tube. Insert the catheter into the endotracheal tube and instil the surfactant in 1-2 boluses as tolerated. FiO2 and peak inspiratory pressure may need to be transiently increased after instillation.

**Criteria for retreatment**

Consider retreatment at 12 hours (6 hours if severe lung disease) if the infant has any oxygen requirement and is unable to be extubated in the near future.

**Adverse Reactions**

Endotracheal tube blockage is a potential complication of surfactant administration. Transient bradycardia and desaturation may occur during the procedure. Increasing the peak inspiratory pressure and FiO2, or giving manual breaths via the ventilator or a bag may help.

A rare complication of surfactant treatment is pulmonary haemorrhage. The risk is tiny compared to the benefits of surfactant treatment. It is likely to be a consequence of increased shunting through a patent ductus arteriosus (PDA), and resultant haemorrhagic pulmonary oedema. Close attention to appropriate ventilatory and PDA management is advised post-surfactant.
References


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