SURFACTANT THERAPY

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Background
Neonatal acute respiratory failure

- Acute respiratory failure is a common problem in preterm and term infants
- In preterm infants, the most common cause of acute respiratory failure is Respiratory Distress Syndrome
- Other secondary causes:
  - Surfactant deficiency in late preterms
  - Infants with Meconium Aspiration Syndrome
  - Pneumonia
  - Sepsis
  - Pulmonary haemorrhage
Respiratory distress syndrome (RDS)

- Primary cause is deficiency of pulmonary surfactant in immature lung
- Affects about 1% of all newborn infants
- Incidence decreases with advancing gestational age, from ~50% in babies born at 26–28 weeks, to about 25% at 30–31 weeks
- Syndrome is more frequent in males, Caucasians, infants of diabetic mothers, and the second born of premature twins
Pulmonary surfactant is composed of:
✓ Lipids (90%) primarily phospholipids
✓ Proteins (10%) SP-B, SP-C, SP-A, SP-D
Surfactant is synthesized within alveolar type II cells
Surfactant is expressed in the lung starting ~20 weeks gestation
Surfactant reduces alveolar surface tension, thereby facilitating alveolar expansion and reducing the likelihood of alveolar collapse atelectasis
Most common cause of surfactant deficiency is preterm delivery.

In infants born at term, mutations in the genes encoding surfactant proteins SP-B and SP-C, as well as Adenosine triphosphate–binding cassette transporter A3 (ABCA3) may cause surfactant deficiency and/or dysfunction.

Clinical manifestations result primarily from abnormal pulmonary function and hypoxemia.

Presents within first minutes or hours after birth.
## Silverman Anderson Scoring System

<table>
<thead>
<tr>
<th>Feature observed</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest movement</td>
<td>Synchronized respirations</td>
<td>Lag on respirations</td>
<td>Seesaw respirations</td>
</tr>
<tr>
<td>Intercostal retraction</td>
<td>None</td>
<td>Just visible</td>
<td>Marked</td>
</tr>
<tr>
<td>Xiphoid retraction</td>
<td>None</td>
<td>Just visible</td>
<td>Marked</td>
</tr>
<tr>
<td>Nares dilation</td>
<td>None</td>
<td>Minimal</td>
<td>Marked</td>
</tr>
<tr>
<td>Expiratory grunt</td>
<td>None</td>
<td>Audible by stethoscope</td>
<td>Audible by unaided ear</td>
</tr>
</tbody>
</table>
- Score 10 = Severe Respiratory Distress
- Score > 7 = Impending Respiratory Failure
- Score 4–6 = Moderate Respiratory Distress
- Score 0–3 = Mild Respiratory Distress
Surfactant
Several clinical trials have shown the benefit of exogenous surfactant administration in preterm infants born less than 30 weeks gestation who are at the greatest risk for RDS\(^1\)

In these trials, surfactant therapy compared with placebo was associated with a lower incidence and severity of RDS and mortality, and a decreased rate of associated complications including bronchopulmonary dysplasia, pulmonary interstitial emphysema and other pulmonary leak complications\(^2\)
Surfactant

- When?
Prophylactic versus Rescue Surfactant

- **Prophylactic, or preventive**, surfactant strategy is defined as intubation and surfactant administration to infants at high risk of developing RDS for the primary purpose of preventing worsening RDS rather than treatment of established RDS.

- Prophylactic doses are administered in the delivery room before initial resuscitation efforts or the onset of respiratory distress or, most commonly, after initial resuscitation but within 10 to 30 minutes after birth.
Rescue or treatment surfactant strategy, in which surfactant is given only to preterm infants with established RDS

It is administered within first 12 hours after birth, when specified threshold criteria of RDS are met
Early versus Delayed Selective Surfactant treatment of RDS

- *Early rescue* is defined as surfactant treatment within 1 to 2 hours of birth, and *late rescue* is defined as surfactant treatment within 2 or more hours after birth.
- Repeat dose is within 4–12hrs if FiO_2_ > 50%.
- A meta-analysis of early versus delayed surfactant treatment concluded that the risk of mortality, air leak, chronic lung disease were significantly decreased in infants given early surfactant treatment.¹
  - There were no differences in other complications of prematurity.
Surfactant

- Which?
Animal derived versus synthetic surfactant

- Treatment with animal derived surfactants has several advantages over first-generation, protein-free synthetic surfactants\(^1\)
- These include lower mortality rates and fewer incidences of pneumothorax.
- Animal derived surfactants contain variable amounts of surfactant protein B (SP–B)
  - SP–B enhances the rate of absorption of phospholipids at the air–water interface, is involved in the formation of tubular myelin, and has anti-inflammatory properties
Natural surfactants are associated with greater early improvement in ventilation support, fewer air leaks and fewer deaths.

These should be given early in the course of RDS.

Several clinical trials have shown natural surfactants to be superior to synthetic preparations; and associated with lower inspired oxygen concentration and ventilator pressures, decreased mortality and lower rate of RDS complications in preterm infants.
Animal derived
- Calfactant (*Infasurf*): bovine calf lung lavage
- Beractant (*Survanta*): bovine lung extract
- Bles: bovine lipid extract
- Poractant alfa (*Curosurf*): porcine lung extract

Synthetic
- Lucinactant (*Surfaxin*): synthetic
- Colfosceril palmitate (*Exosurf*): synthetic
Surfactant

How?
Modes of delivering surfactant

1. Endotracheal intubation
   - Bolus administration
     - One dose
     - Multiple doses (in aliquots)
   - Continuous infusion
2. Less invasive:

- Aerosolized surfactant preparations
- Laryngeal mask airway–aided delivery of surfactant
- Pharyngeal instillation
- Use of intratracheal catheters
3. MIST (Minimally Invasive Surfactant Therapy)

- Minimizes airway injury
- Avoids placing positive pressure ventilation (PPV) on immature lungs
- The breathing preterm baby with RDS receives surfactant via gastric tube placed in the trachea
Dose

- Animal derived
  - 4mls/kg (4 aliquots)

- Synthetic
  - 2.5–3mls/kg (2 aliquots)
Criteria for surfactant administration

1. Extreme preterms
   - Intubate immediately after birth and surfactant is given prophylactically

2. Infants initially treated with non-invasive ventilation (nCPAP)

3. \( \text{FiO}_2 > 40\% \) to maintain \( \text{SPO}_2 > 88\% \) or \( \text{PaO}_2 > 45\text{mmHg} \)

4. \( \text{PaO}_2 > 55\text{mmHg} \) to 60mmHg with pH < 7.25
5. Repeated apneas, requiring bag and mask ventilation

6. Significant work of breathing, retractions, grunting, increased anteroposterior diameter (ref. to Silvermann–Anderson score chart)
Recommendations

- Indications as per 2014 American Academy of Paediatrics (AAP) and the European Consensus Guidelines (ECG) recommendations, is to initially provide nCPAP to all patients with RDS, and intubate and administer surfactant to those with persistent severe respiratory distress (defined as requiring a fraction of inspired oxygen [FiO₂] of 0.40 or higher to maintain oxygen saturation above 90%) or who are apneic.
Additional doses of surfactant therapy are administered if the patient has a persistent requirement of an \( \text{FiO}_2 > 0.30 \).

Rescue surfactant may be considered for infants with hypoxic respiratory failure (due to pulmonary haemorrhage, MAS, sepsis, pneumonia).

- Intubated infants with MAS requiring >50% oxygen should receive exogenous surfactant therapy.
Limited data in preterm infants with severe RDS requiring mechanical ventilation suggest that combination of surfactant and budenoside (corticosteroid) reduced the incidence of BPD and the composite outcome of death and BPD\(^1\). However there was no difference in mortality.
INSURE Procedure

- Intubate
- Surfactant
- Extubate

INSURE is preferred for non-intubated infants with:
- Clinical RDS
- Abnormal CXR
- Worsening FiO₂ requirement
Infants should have good respiratory effort

Infants should be < 6 hours old

Infants NOT good for INSURE:

- Those intubated at birth for apneas and poor respiratory effort
- Neonates who have received extensive resuscitation
- Any associated medical issues e.g. anemia, hydrops, asphyxia, etc
Administer surfactant procedurally then extubate to nCPAP

Before extubation ensure:
- HR and SPO$_2$ are stable
- FiO$_2$ less than the pre-surfactant level (<30%)
- No apneas
- Adequate airflow without clinical evidence of airway obstruction
Increasingly non-invasive respiratory support through nCPAP is associated with a decreased risk of developing chronic lung disease compared with conventional mechanical ventilation.

Meta-analysis of nCPAP with/without INSURE tend to favour early INSURE over nCPAP alone for reducing BPD, air leak, death.

Some infants (30%-50%) still require mechanical ventilation.
Complications of surfactant administration:

- Transient hypoxia
- Transient bradycardia
- ETT blockage
- Air leaks
- Oxygen desaturations
- Pneumothorax (sudden changes in pulmonary compliance)
- Pulmonary haemorrhage (low incidence)
Other Indications of surfactant use

1. Pulmonary haemorrhage\(^1\)
2. Meconium aspiration syndrome
3. Congenital diaphragmatic hernia\(^2\)
4. Critically ill infants with RSV bronchiolitis\(^3\)

\textbf{NB}: Incidences of other medical morbidities (BPD, IVH, NEC, ROP, PDA, Infections) have not changed with surfactant therapy
Merci beaucoup**

Dieu  Vous  Protégé!