Guideline

Women and Babies:  Surfactant in Term Infants

Document No:  RPAH_GL2016_025
Functional Sub-Group:  Clinical Governance
Summary:  Early surfactant replacement treatment should be considered for ventilated term infants with conditions associated with surfactant deficiency or inactivation (including meconium aspiration syndrome).

National Standard:  
- Standard 1:  Governance for Safety and Quality in Health Service Organisations
- Standard 9:  Recognising and Responding to Clinical Deterioration in Acute Health Care

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Compliance with this Guideline is recommended
Women and Babies: Surfactant in Term Infants

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1. INTRODUCTION
Surfactant deficiency or inactivation is a component of respiratory distress in near-term infants (37, 38 weeks) delivered without labour and as a complication of several respiratory diseases in term infants.

The risks addressed by this policy:
Clinical risk of respiratory failure in term infants.

The aims / expected outcome of this policy
Surfactant deficiency or inactivation will be recognised early and surfactant replacement treatment given where appropriate.

2. GUIDELINE STATEMENT
Exogenous surfactant treatment should be considered in term infants with meconium aspiration syndrome (MAS), with respiratory failure and infants on ECMO.

3. PRINCIPLES/GUIDELINES
3.1 Summary
- Surfactant deficiency and/or inactivation are associated with MAS, persistent pulmonary hypertension (PPHN), transient tachypnoea of the newborn (TTN), neonatal encephalopathy, neonatal acute respiratory distress syndrome (ARDS) and pneumonia in term infants.
- Benefits of exogenous surfactant have been shown in randomised controlled trials (RCT) in term infants with MAS, with respiratory failure and infants on ECMO.

3.2 What we do at RPA
Infants born near term or term at risk of respiratory distress syndrome should have surfactant treatment immediately after intubation. Consider surfactant for ventilated infants if:
- Born by elective caesarean section before 39 weeks particularly if the mother did not receive antenatal corticosteroids.
- A chest x-ray is consistent with respiratory distress syndrome.
- The click test is negative or equivocal.
- With meconium aspiration syndrome if FiO$_2$ ≥0.4.

Treatment:
Respiratory distress syndrome: give Curosurf 200 mg/kg then 100 mg/kg every 6 to 12 hours until extubated to a maximum of 4 doses depending on respiratory compliance.

- Meconium aspiration syndrome: give Curosurf 150 mg/kg every 6 to 12 hours until infant in less than 40% oxygen to a maximum of 4 doses.
3.2 Incidence

Table 1 reports the risk of serious respiratory morbidity or mechanical ventilation in population cohorts of near term (37, 38 weeks gestation) and term infants.

<table>
<thead>
<tr>
<th></th>
<th>Years</th>
<th>n</th>
<th>37</th>
<th>38</th>
<th>39</th>
<th>40</th>
<th>41</th>
<th>≥42</th>
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<tr>
<td>Mechanical ventilation</td>
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<td>0.4</td>
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<td>1st day %</td>
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<tr>
<td>%</td>
<td>2003</td>
<td>2527766</td>
<td>0.57</td>
<td>0.32</td>
<td>0.28</td>
<td>0.29</td>
<td>0.38</td>
<td></td>
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<tr>
<td>Serious respiratory</td>
<td>1990-1998</td>
<td>14531</td>
<td>1.4</td>
<td>1.1</td>
<td>0.7</td>
<td>0.8</td>
<td>1.1</td>
<td>1.6</td>
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<td>morbidity %</td>
<td>1998-2006</td>
<td>34458</td>
<td>1.9</td>
<td>0.9</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>Serious respiratory</td>
<td>2003</td>
<td>2527766</td>
<td>0.57</td>
<td>0.32</td>
<td>0.28</td>
<td>0.29</td>
<td>0.38</td>
<td></td>
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<td>morbidity in elective</td>
<td>1998</td>
<td>34458</td>
<td>1.9</td>
<td>0.9</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>caesarean deliveries %</td>
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<td>2527766</td>
<td>0.57</td>
<td>0.32</td>
<td>0.28</td>
<td>0.29</td>
<td>0.38</td>
<td></td>
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<tr>
<td>Serious respiratory</td>
<td>2003</td>
<td>2527766</td>
<td>0.57</td>
<td>0.32</td>
<td>0.28</td>
<td>0.29</td>
<td>0.38</td>
<td></td>
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<tr>
<td>morbidity in intended</td>
<td>1998-2006</td>
<td>34458</td>
<td>1.9</td>
<td>0.9</td>
<td>0.2</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
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<td>vaginal deliveries %</td>
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<td>2527766</td>
<td>0.57</td>
<td>0.32</td>
<td>0.28</td>
<td>0.29</td>
<td>0.38</td>
<td></td>
</tr>
</tbody>
</table>

3.3 AETIOLOGY AND RISK FACTORS:

Common respiratory diagnoses at near term gestation (37 and 38 weeks) are respiratory distress syndrome\(^1,5-8\) and transient tachypnoea of the newborn\(^8\). The term infant is at lowest risk of respiratory morbidity,\(^3,4,7-11\) with common diagnoses including persistent pulmonary hypertension, transient tachypnoea of the newborn, congenital pneumonia, pneumothorax and meconium aspiration syndrome.\(^5\) Postmature infants (≥42 weeks’ gestation) are at increased risk of perinatal asphyxia and meconium aspiration syndrome.\(^4,5,12\)

Antecedents to these diagnoses include clinical presentations associated with prematurity increasing the likelihood of lung immaturity (respiratory distress syndrome) and infection, preterm rupture of membranes or clinical chorioamnionitis increasing the likelihood of infection, and postmature delivery with meconium stained liquor - meconium aspiration syndrome. Infants born by elective caesarean section, especially before 39 weeks gestation, are at much higher risk of respiratory distress syndrome.\(^1,3,5,6,8\)

3.4 DIAGNOSIS:

Surfactant deficiency may be suspected in term infants if a condition known to be associated with surfactant dysfunction is present. The diagnostic accuracy of a chest x-ray diagnosis of respiratory distress syndrome (fine granularity, air bronchograms and low lung volume) has not been reported. Surfactant deficiency or inactivation is diagnosed by performing the click test on a tracheal aspirate as soon as possible after intubation of any infant with respiratory distress.\(^13-15\) In a cohort of term ventilated infants, surfactant dysfunction (negative or equivocal test) was consistently seen in respiratory distress syndrome (RDS), transient tachypnea of the newborn, and severe meconium aspiration syndrome (MAS).\(^13\) Infants with meconium aspiration syndrome requiring FiO\(_2\) > 0.4 were reliably shown to have surfactant inactivation (negative click
3.5 CONSEQUENCES (PROGNOSIS)

Near term and term infants who develop respiratory failure are at increased risk of mortality and neurodevelopmental impairment. In a trial of early nitric oxide for ventilated infants born ≥34 weeks gestation with an oxygenation index ≥15 and <25, 89% survived to age 18 to 24 months, with neurodevelopmental impairment rates 25-27%, hearing impairment 23% - 24% and psychomotor developmental index scores 89; (sd 17.7) - 93.5 (18.4).16

3.6 INTERVENTIONS:

Prevention

- Preventing respiratory morbidity at term gestation: A high proportion of pregnancies are delivered electively (induction of labour or caesarean section) near or at term for maternal or foetal indications. Elective caesarean section at near term gestation (37-38 weeks) carries a moderate risk of respiratory morbidity in the infant,5, 6, 8, and substantially higher risk than intended vaginal delivery.6
- Trials of use of antenatal corticosteroids at near term and term gestations have reported a reduction in respiratory morbidity.17-19 However, clinical guidelines conclude there is insufficient evidence from trials to recommend routine use of antenatal corticosteroids at or near term.17
- Delaying delivery until 39 weeks gestation is associated with lowest incidence of respiratory morbidity17-19 and combined perinatal and infant mortality.20
- Induction of labour for improving birth outcomes for women at or beyond term: Induction of labour at our beyond term reduces perinatal mortality (17 trials, 7407 infants; RR 0.31 95% CI 0.12, 0.81) and meconium aspiration syndrome (8 trials, 2371 infants; RR 0.50, 95% CI 0.34, 0.73).21 There were also fewer caesarean sections in the induction group compared with the expectant management group. The majority of trials adopted a policy of induction at 41 completed weeks (287 days) or more.

Treatment

- **Surfactant for meconium aspiration syndrome:** Surfactant treatment of ventilated infants with meconium aspiration syndrome did not affect mortality, pneumothorax, air leak or duration of mechanical ventilation, but reduced requirement for ECMO (2 trials, 208 infants; RR 0.64, 95% CI 0.46, 0.91).22 The trials that reported benefit in respiratory parameters and prevention of ECMO gave 100-150 mg/kg surfactant every 6 hours for 4 doses, with infants treated earlier having the greatest response.23, 24
- **Dilute surfactant lung lavage for meconium aspiration syndrome:** did not affect mortality, treatment with ECMO, or pneumothorax but reduced combined mortality and treatment with ECMO (2 trials, 88 infants; RR 0.33, 95% CI 0.11, 0.96).25 There are no trials reporting the comparison of surfactant treatment compared to dilute surfactant lung lavage in infants with meconium aspiration.
### Table 2: Surfactant in full term / near term infants:

<table>
<thead>
<tr>
<th></th>
<th>Mortality</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfactant for meconium</td>
<td>4 / 326</td>
<td>0.98</td>
<td>[0.41, 2.39]</td>
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<tr>
<td>aspiration syndrome in</td>
<td>Treatment with ECMO</td>
<td>2 / 208</td>
<td>0.64</td>
</tr>
<tr>
<td>full term / near term</td>
<td>Chronic lung disease</td>
<td>1 / 168</td>
<td>0.47</td>
</tr>
<tr>
<td>infants</td>
<td>Pneumothorax / air leak</td>
<td>3 / 269</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>Days mechanical ventilation</td>
<td>3 / 158</td>
<td>0.60</td>
</tr>
<tr>
<td>Lung lavage for meconium</td>
<td>Mortality</td>
<td>2 / 88</td>
<td>0.42</td>
</tr>
<tr>
<td>aspiration syndrome in</td>
<td>Treatment with ECMO</td>
<td>2 / 47</td>
<td>0.27</td>
</tr>
<tr>
<td>newborn infants</td>
<td>Mortality or use of ECMO</td>
<td>2 / 88</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Pneumothorax</td>
<td>2 / 88</td>
<td>0.38</td>
</tr>
</tbody>
</table>

### 4. Key Points

- Ventilated term infants are at risk of surfactant deficiency. Consider performing a click test to determine presence or absence of functioning surfactant.
  - Level of evidence IV\(^{13-15}\)
  - Strength of recommendation C

- Ventilated near term and term infants with respiratory failure are at increased risk of mortality and disability.
  - Level of evidence III\(^{16}\)
  - Strength of recommendation B

- Respiratory morbidity at term is reduced by:
  - Delaying elective caesarean delivery to 39 weeks;\(^{5-8}\)(LOE III-1; GOR B)
  - Antenatal corticosteroids prior to elective caesarean section at term where considered appropriate;\(^{17-19}\)(LOE II, GOR C) and

- Induction of labour at 41 completed weeks. (LOE I, GOR A)

- Surfactant treatment of ventilated infants with meconium aspiration syndrome reduced requirement for ECMO and improved respiratory parameters. Give 150 mg/kg surfactant every 6 hours for 4 doses, with infants treated earlier having the greatest response.
  - Level of evidence I
  - Strength of recommendation B

- Dilute surfactant lung lavage for meconium aspiration syndrome did not affect mortality, treatment with ECMO, or pneumothorax but reduced combined mortality and treatment with ECMO.\(^{25}\)(LOE 1) There are no trials comparing dilute surfactant lavage to
  - Level of evidence IV
  - Strength of recommendation C
surfactant replacement in infants with MAS so its role in management of MAS is unclear.

5. PERFORMANCE MEASURES

- Surfactant use and time to surfactant in ventilated term infants with RDS and MAS.
- Mortality and duration of mechanical ventilation of infants born at term gestations.

6. DEFINITIONS:

- **Meconium aspiration syndrome**: presence of early onset respiratory distress in an infant born through thick meconium stained liquor, where meconium has been aspirated from below vocal cords and / or a chest x-ray shows patchy infiltrates.

- **Respiratory distress syndrome**: presence of early onset respiratory distress in an infant with a typical chest x-ray (fine granularity, air bronchograms, low lung volume) and/or evidence of surfactant deficiency (eg negative or equivocal click or stable microbubble test).

7. REFERENCES AND LINKS