North Trent Neonatal Network Clinical Guideline

Title: Pulmonary Haemorrhage (neonatal)
Author: Elizabeth Pilling (adapted from P Adiotomre and R Kacheroo)
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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the North Trent Neonatal Network. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Best practice recommendations represent widely used evidence-based practice and high quality standards that all Neonatal Units across the Network should implement. Subsequent suggested recommendations may be put into practice in local units. However, alternative appropriate local guidelines may also exist.

A. Summary page
1. Aim of guideline
The aim of this guideline is to provide evidence based management of significant pulmonary haemorrhage in infants.

2. Minimum standards where appropriate
As a minimum, neonatal units should have a guideline for the management of pulmonary haemorrhage.

3. Summary

Summary of management:

Minor haemorrhage
- Close monitoring
- Avoidance of suctioning

Major haemorrhage

Immediate management:
Manage airway, breathing and circulation
- Intubate and avoid removing ET tube
- Avoid suction
- Increase pressures and inspiratory time
- In shocked infants, provide circulatory support with blood product replacement

Subsequent management
- Monitor blood gases
- In hypoxic infants, consider a dose of surfactant (200mg/kg)
• Manage hypotension (as per NTNN guideline)
• Correct haematological parameters (see NTNN guideline)
• Treat for sepsis
• Closely monitor and manage fluid balance—consider fluid restriction and diuretics
• In infants with massive haemorrhage, consider endotracheal adrenaline (see text)

B. Full guideline

1. Background
Pulmonary haemorrhage is a relatively common but serious complication seen predominantly in preterm infants.

The incidence of pulmonary haemorrhage is 1-12 per 1000 live births. The median age at onset is 46 hours for the preterm baby born at 34 weeks and below. However for the near term or full term baby born after 34 weeks of gestation the median age at onset is 6 hours.

The 18 month outcomes of infants following a serious pulmonary haemorrhage were significantly worse (incidence of death or neurosensory impairment of 75% compared to 43% in matched infants without haemorrhage, OR 3.36).

2. Aim
The aim of this guideline is to provide evidence based management of significant pulmonary haemorrhage in infants.

3. Areas outside remit if applicable
Management of insignificant pulmonary haemorrhage

4. Core guideline

4.1 Aetiology
The lung effluent of infants with pulmonary haemorrhage has a low haematocrit and small molecular weight proteins, leading to the conclusion that the majority of cases, it is due to haemorrhagic oedema rather than whole blood.

The pathogenesis of PH is therefore considered to be alveolar overdistension with high pulmonary capillary pressure causing epithelial breaks and leakage into the air spaces. This is thought to be caused by overdistention of the alveoli by mechanical ventilation and increased pulmonary capillary pressure due to a patent ductus arteriosis. There is circumstantial evidence to support this, with the risk factors associated with PH including ventilation, prematurity, PDA.

4.2 Risk factors

Risk factors for development of pulmonary haemorrhage are:
For preterm infants

• Preterm birth
• Lack of antenatal steroids
• Need for positive pressure ventilation
• Surfactant therapy
• Patent ductus arteriosus
• Thrombocytopenia (<100x10^6)

For term infants
• Hypoxia
  o In utero (i.e. infants with growth restriction)
  o Intrapartum (i.e. infants with hypoxic ischaemic encephalopathy)
  o Post partum (e.g. infants with meconium aspiration syndrome, difficult intubation leading to hypoxia)
• Delivery room resuscitation with positive pressure ventilation
• Hypotension

4.3 Prevention

Antenatal
Use of antenatal steroids in women at risk of preterm birth

Respiratory
Avoidance of hypoxia (especially in term infants who require resuscitation)
Avoidance of “unnecessary” doses of surfactant. (see NTNN RDS guideline)

Cardiovascular
Management of hypotension (see NTNN hypotension guideline)
Management of PDA (see NTNN guideline)
Avoidance of fluid overload (as this increases risk of PDA)

4.4 Diagnosis
There is considerable debate in the literature about the diagnostic criteria of pulmonary haemorrhage. Many infants have blood streaked endotracheal aspirates, however these frequently represent local trauma rather than significant haemorrhage. In the TIPPS^4 trial 15.6% of infants had some blood aspirated from the endotracheal tube, however 10.2% of infants had “serious” pulmonary haemorrhage, defined as requiring increase in ventilator support, oxygen requirement or blood product replacement.

Table 1 describes the clinical differences and actions:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Significant pulmonary haemorrhage</th>
<th>Minor pulmonary haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suction findings</td>
<td>Copious amounts of fresh blood</td>
<td>Minimal staining of ET secretions with fresh or old blood</td>
</tr>
<tr>
<td>Clinical observations</td>
<td>Tachycardia, ↓BP, Pallor Acute deterioration in ventilation</td>
<td>No signs of acute deterioration</td>
</tr>
<tr>
<td>Management</td>
<td>Most likely diagnosis - traumatic bleeding Suggest minimal suctioning and watch for clinical deterioration</td>
<td></td>
</tr>
</tbody>
</table>
A chest x-ray taken at the time will show patchy changes (the blood), signs consistent with heart failure. If there is a massive haemorrhage, complete “white out” maybe seen due to obstruction of the endotracheal tube with blood clots.

4.5 Treatment

4.5.1 Minor pulmonary haemorrhage

This may be a precursor to major haemorrhage, therefore the infant should be closely monitored and wherever possible suction and re-intubation avoided.

4.5.2 Significant pulmonary haemorrhage

Infants with massive PH can be acutely unwell with hypovolaemic shock.

4.5.2a) Assess as ABC:

- **Airway**
  If the infant is not intubated this will be necessary. However, this can be difficult due to haemorrhage. The most experienced intubator should perform this procedure in this situation (see NTNN guideline). Note end tidal CO$_2$ monitoring may be unhelpful in this situation as it may be falsely negative.

  In infants who are intubated, avoid removing the endotracheal tube, as replacing it can be extremely difficult. If the tube is completely blocked with blood, suction may be necessary. However, wherever possible, this should be avoided as it can precipitate further haemorrhage.

- **Breathing**
  There may be significant hypoxia during haemorrhage. The mean airway pressure should be increased. This can be achieved by increasing the PEEP (e.g. 6-7), inspiratory time (e.g. 0.4-0.5), PIP (or tidal volume if on VG) in steps. This helps by redistributing the lung fluid into the interstitial spaces and improving ventilation. High frequency oscillation can also be used in this situation where available.

- **Circulation**
  Infants with significant haemorrhage are often bradycardic and hypotensive. Blood replacement may be required urgently depending on the degree of haemorrhage. However note that the cause of PH is usually pulmonary oedema, therefore avoidance of further fluid overload is important. Wherever possible, “useful” fluid replacement should be given e.g. blood products, rather than saline.

  Hypotension should be managed as per NTNN guideline with the early use of inotropes.
4.5.2b) Further therapy

Once the infant is acutely stabilised the following therapies can be considered:

- **Respiratory**

  **Surfactant**
  - There are no randomised controlled trials looking at the use of surfactant in PH, however there are a number of observational studies. A dose of 200mg/kg is used, once the infant has been stabilized if they still have a significant oxygen requirement. This is thought to act by replacing the surfactant inactivated by haemorrhage.

  - **Blood gases**
    Close monitoring of blood gases is necessary following significant pulmonary haemorrhage. Correction of acidosis may be needed, but this should be done once the other causes have been treated (e.g. hypotension). Note that bicarbonate boluses may contribute to further haemorrhage by increasing volume overload.

- **Sedation/muscle relaxation**
  - If ventilation is difficult, and the baby is unsettled, sedation and muscle relaxation may be required for a short period of time to allow for physiological stability to be achieved.

- **Cardiovascular/Haematology**
  - Urgent samples should be taken for coagulation studies and full blood count. Correction may be required (see NTNN guidelines). Again, caution is needed with excessive fluid correction.

- **Fluids**
  - Once the infant is cardiovascularly stable, fluid restriction and diuretics may be indicated to reduce the risk of fluid overload.

- **Sepsis**
  - Sepsis may be the cause of PH, and therefore blood cultures should be taken and appropriate antibiotics commenced.

4.5.2.c) Other therapies

- **Adrenaline**- there is one longitudinal study using endotracheal adrenaline. The theoretical method of action is in constricting arterioles and reducing haemorrhage. There was a statistically significant improvement in survival in the group given adrenaline, but they were compared to historical controls and the treatment group included just 5 infants. 1:10,000 adrenaline of 0.3-1ml/kg was given via catheter advanced through the endotracheal tube (i.e. like surfactant). (REF)

- **Hemocoagulase**- One study has been published with 28 infants treated with hemocoagulase. This demonstrated a
significant reduction in mortality, however this drug is not currently available in the UK.

- Cocaine- using a 4% cocaine spray (as used in some ENT departments) to promote vasoconstriction has been used in 1 study\(^7\) however there is some concern regarding the use of cocaine in newborns and in addition it can be difficult to source.

6. Audit criteria
None identified

7. References

1. Ductal Shunting, high pulmonary blood flow and pulmonary haemorrhage. Kluckow Journal of Pediatrics 136 (1) 68


C. Appendices

1. Evidence grading