The Yorkshire and Humber Neonatal Operational Delivery Network

NHS

Yorkshire & Humber Neonatal Network (South) Clinical Guideline

Title: Pulmonary Haemorrhage (Neonatal)

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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire & Humber Neonatal ODN (South). 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.

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
- Check full blood count/clotting screen- correct as appropriate any clotting abnormalities (see Y&H ODN (South) guideline)

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 Y&H ODN (South) guideline)
- Correct haematological parameters (see Y&H ODN (South) guideline)
- Treat for sepsis
- Closely monitor and manage fluid balance- consider fluid restriction and diuretics
- In infants with massive haemorrhage, consider endotracheal adrenaline

B. Full guideline

1. Background

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

There are many definitions, however a working definition would be the appearance of fresh blood in the ET tube/ trachea accompanied by a clinical deterioration.

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[1].

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]

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 exact cause remains unknown. The lung effluent of infants with pulmonary haemorrhage has a low haematocrit and small molecular weight proteins, leading to the conclusion that in most cases, it is due to haemorrhagic oedema rather than whole blood.

The pathogenesis of PH is therefore considered to be alveolar over distension 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 arteriosus. There is circumstantial evidence to support this, with the risk factors associated with PH including ventilation, prematurity, PDA[3].

4.2 Risk factors[1,4]

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 ($<100x10^6$)
- IUGR

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

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 Y&H Neonatal ODN (South) RDS guideline)

Cardiovascular
Management of hypotension (see Y&H Neonatal ODN (South) hypotension guideline)
Management of PDA (see Y&H Neonatal ODN (South) 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[5] 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.

Clinical

Identification of risk factors with pink frothy fluid at the ET tube should prompt the suspicion of PH. The typical presentation is a premature infant who suddenly presents with frothy pink tinged secretions from an ET. Over the next minutes to hours, the infant often requires increased ventilatory support and has increased work of breathing

Diagnosis	**Significant pulmonary haemorrhage**	**Minor pulmonary haemorrhage**
Suction findings	Copious Amounts of fresh blood	Minimal staining of ET secretions with fresh or old blood
Clinical observations	Tachycardia, ↓BP, Pallor Acute deterioration in ventilation	No signs of acute deterioration
Management	**See below**	Most likely diagnosis - traumatic bleeding Suggest minimal suctioning and watch for clinical deterioration

Radiology

A chest x-ray may be nonspecific (3). Based on the severity and timing of PH, the x-ray 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.

Investigations

- Full Blood Count
- Crossmatch
- Coagulation screen
- Blood gas (hypoxia, hypercarbia, metabolic acidosis)
- Biochemical profile
- C-reactive Protein (CRP)
- Blood culture
- Cranial ultrasound scan – intraventricular haemorrhage may be an association
- Echocardiography – to assess PDA and left ventricular function

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.

Initial Management
Assess as ABC:

Ventilation:

a) If the infant is not intubated, this will be necessary. However, this can be difficult due to haemorrhage. The member of staff most experienced at intubation should perform this procedure in this situation. Note end tidal CO_2 monitoring may be unhelpful in this situation as it may be falsely negative.

b) 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 and to ensure that blood clots have not blocked the tube, suction may be necessary. However wherever possible, this should be avoided as it can precipitate further haemorrhage.

c) There may be significant hypoxia during haemorrhage. The mean airway pressure should be increased. This can be achieved by increasing the PEEP (e.g., 6-8, 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. PEEP may provide tamponade of the pulmonary capillaries

d) High frequency oscillation can also be used in this situation where available[6].

e) 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.

f) 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.

g) Surfactant

There are no randomised controlled trials looking at the use of surfactant in PH, however there are a number of observational/ retrospective 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[7]. No conclusions can be made based on these trials regarding the use of surfactant (14)

- **Cardiovascular support:**

a) 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.

b) Hypotension should be managed as per Y&H Neonatal ODN South guideline with the early use of inotropes.

c) Urgent samples should be taken for coagulation studies and full blood count. Correction may be required (see Y&H Neonatal ODN South guidelines). Again, caution is needed with excessive fluid correction.

d) An echocardiograph should be done to rule out left to right shunting through a PDA

- **Fluids**

Once the infant is cardiovascularly stable, fluid restriction and diuretics may be indicated to reduce the risk of fluid overload. Fluid restriction is beneficial for management of PDA which is one of the major risk factors for PH. (15)

- **Sepsis**

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

- **Coagulopathy**

It is not uncommon for secondary DIC to occur following a massive PH. If clotting parameters are found to be deranged, fresh frozen plasma can be used for volume replacement.

4.5.3 Other therapies

These have with very limited evidence base but are detailed below. It may be appropriate to consider use of these therapies following discussion with a tertiary centre neonatologist when other therapies have not been successful.

- Adrenaline
  The theoretical method of action is in constricting arterioles and reducing haemorrhage. There is a longitudinal study[8] using endotracheal adrenaline. 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). A further retrospective study published in 2013[9] gave 0.5ml of adrenaline (1 in 10,000) with 1ml of air using a 5ml syringe through an oral gastric tube. The authors gave the adrenaline after every suction and tried to create a 'force injection'. Suction was only used if there was dyspnea, hypercapnia or hypoxemia. In this study, it was felt that the adrenaline' spraying' had an affect by the third to fifth dose. This study was completed on 18 VLBW neonates with severe pulmonary haemorrhage.

- Hemocoagulase
  One study[10] 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. There have been no RCTs looking at the effectiveness of this drug.

- Cocaine
  Using a 4% cocaine spray (as used in some ENT departments) to promote vasoconstriction has been used in 1 study[11] however there is some concern regarding the use of cocaine in newborns and in addition it can be difficult to source.

- Activated recombinant factor VII (rfVIIa)
  This is used in patients with severe haemophilia A and B who are bleeding. It has been used to treat severe PH which is refractory to conventional ventilator management in VLBW neonates. There have been case studies reported[12] describing two babies in which it was successful is controlling bleeding. There has also been a retrospective cohort study[13] which comprised 18 infants (16 of which were premature) including 5 with pulmonary haemorrhage. Haemostasis was achieved in all infants with PH after 1-3 doses of 90 micrograms/kg. In the cohort, there was a baby diagnosed with a non-occlusive aortic thrombus on ultrasound (had also had a UAC in-situ). In adults, high dose rFVIIa has been associated with cerebral venous thrombosis, although there has not been a case reported in newborns.

6. Audit criteria
None identified

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