Pulmonary Haemorrhage in Neonates

University Hospitals of Leicester NHS Trust

Trust ref: C5/2011

1. Introduction and Who Guideline applies to

This guideline is aimed at all Health care professionals involved in the care of infants within the Neonatal Service.

Aim:

To provide evidence-based recommendations on the recognition and management of pulmonary haemorrhage (PH).

Key Points:

1	Neonates who develop pulmonary haemorrhage are critically ill and require appropriate resuscitation.
2	High frequency oscillatory ventilation may be useful as rescue therapy in neonates with massive pulmonary haemorrhage who are not responding to conventional ventilation. *Grade of Evidence: B*
3	Administration of natural surfactant in neonates presenting with pulmonary haemorrhage may result in improvement of respiratory function. *Grade of Evidence: B*
4	There is often associated hypovolemia and shock which may need prompt correction by packed cell transfusion and/or fresh frozen plasma (FFP). *Grade of Evidence: C*
5	There is little available evidence on the effects of fluid restriction or the use of diuretics in babies who have suffered a pulmonary haemorrhage. *Grade of Evidence: C*

Related UHL documents:

Patent Ductus Arteriosus PDA in Preterm Babies UHL Neonatal Guideline Trust ref: C14/2007
Red Cell Transfusion UHL Neonatal Guideline Trust ref: C165/2008

2. SUPPORTING INFORMATION

Background

Pulmonary haemorrhage (PH) can be defined as an acute, cata-strophic event which is characterised by discharge of bloody fluid from the upper respiratory tract or the endotracheal tube. The most common risk factor associated with PH is prematurity. PH is typically be seen in babies weighing less than 1500g, who often have a patent ductus arteriosus (PDA), have been treated with surfactant and are ventilated[1]. The incidence of PH is 1 to 12 per 1,000 live births with PH occurring most commonly within the first few days of life[2]. Other risk factors predisposing to PH include intrauterine growth restriction, chorioamnionitis, coagulopathy and respiratory disorders[3].The typical presentation of the infant with PH is in an extreme premature infant with sudden onset of frothy, pink-tinged secretions or frank bleeding from the endotracheal tube, often requiring increased ventilatory support. If the PH continues, the infant can develop apnoea, generalised pallor, become cyanotic, with con-comitant bradycardia and hypotension from hypovolaemic shock[4] Mortality rates as high as 50% have been reported in extremely pre-mature neonates and there is currently no curative treatment that exists for PH in neonates, although numerous studies have identified treatments that have been shown to increase survival rates.

To date, no systematic review exists to outline the best management of neonatal pulmonary haemorrhage (PH). Most observations have been based on observational cohort studies, case series and reports. Future randomised control trials will be essential to further deduce the most effective management of PH.

Diagnosis

Clinical

PH is usually diagnosed clinically, although only a small percentage of PH evident at autopsy are manifest clinically [5]. It often presents on day 2-4 of life. History should focus on identification of predisposing risk factors (infection, PDA), whilst examination reveals pink or red frothy fluid in the airway. The baby is often acutely unwell, hypoxic, in severe respiratory distress, bradycardic, collapsed, pale and shocked. If ventilated, there may be haemorrhagic fluid in the trachea with cardiorespiratory decompensation. It is important to remember that recent/traumatic intubation may also lead to small amounts of blood-tinged fluid on suctioning of the endotracheal tube, which should not be mistaken for pulmonary haemorrhage. If not ventilated, the baby may be apneic with blood-tinged fluid seen on laryngoscopy.

Radiological

Radiological changes may be acute but non-specific. A chest x-ray may show focal (patchy infiltrates, fluffy opacities, nodular densities or focal ground-glass opacities) or massive (lung field ‘whiteout’ with air bronchograms) changes.

Laboratory

Haematocrit of the haemorrhagic oedema fluid is usually <10%. If this is higher, pulmonary haemorrhagic oedema is unlikely and the blood may be traumatic in nature, due to disseminated intravascular coagulopathy (DIC) or swallowed maternal blood.

Investigations

Investigations address cardiopulmonary compromise associated with acidosis (metabolic or mixed), a deficit in haematocrit and a possible coagulopathy.

- Full Blood Count
- Crossmatch
- Coagulation screen (often not causal)
- 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

Management (Appendix 1)

PH can be associated with high mortality and these babies are usually very sick. Massive PH can be life-threatening. Aim to prevent exsanguination whilst ensuring simultaneous gas exchange [6].

Always inform the Consultant Neonatologist if suspecting or treating a baby for PH.

Resuscitation is key – follow the principles of 'ABC'.
Restore haemodynamic stability.
Correct acidosis.
Consider the possibility of sepsis.

Ventilatory Strategy:

All babies must be mechanically ventilated, with oxygen administration guided by oxygen saturation.

Suctioning of the airway as required to remove haemorrhagic fluid, but limit aggressive suctioning.

During massive PH, the view of the vocal cords may be obscured, thus leading to difficulty with endotracheal intubation. If the baby is already intubated, **do not remove the endotracheal tube** unless it is blocked. If the baby needs intubation,

this can be technically difficult due to the presence of haemorrhagic fluid/blood in the trachea and airways. In such conditions use of Boogie from the difficult airway kit can be useful [7]

Ventilatory strategies must include providing high mean airway pressures, which may need high PIP (up to 30cm of water may be necessary, guided by chest movement and blood gases) and high PEEP (6-8 cm of water) to provide tamponade of the high pulmonary capillary pressures by distending the airways [8].

High Frequency Oscillatory Ventilation (HFOV):

In babies with massive PH and severe respiratory failure, which is not responding to conventional ventilation, consider the use of HFOV after discussion with a Consultant Neonatologist.
There is some evidence, in the form of observational cohort studies [9,10] involving small numbers, showing a statistically significant decrease in oxygenation indices and oxygen requirements in the babies who responded to the use of HFOV as rescue therapy. In view of the lack of randomized controlled trials, it is uncertain whether providing a high mean airway pressure whilst limiting tidal volume excursions with HFOV is superior to conventional ventilation in minimizing interstitial and alveolar fluid accumulation. HFOV should be considered as rescue therapy after discussion with a Consultant Neonatologist.
Paralysis and/or sedation may be necessary if the infant is not synchronizing with the ventilator and adequate control is required.

Use of Surfactant:

Consider the use of a single dose of surfactant (Curosurf: dose 100-200 mg/kg, give the dose i.e. 120 mg/240 mg/360 mg/480 mg after rounding off to the higher value) in babies with difficult ventilation after discussion with a Consultant Neonatologist.
There have been association between PH and surfactant [11-15]. Paradoxically, surfactant has been used as adjuvant therapy in PH. Administration of curosurf in neonates presenting with pulmonary haemorrhage may result in improvement of respiratory function [16-20] A Cochrane Systematic Review [21] concluded that although there was potential benefit of surfactant in the management of PH, there was an inability to make recommendations in the absence of randomized controlled trials.

Cardiovascular Support

PH may be associated with hypotension and anaemia. This needs prompt recognition and may need management by volume replacement in the form of blood products (packed red cells) and may also involve the use of inotropes.

Fluid management

There is very little evidence on guidance regarding fluid management or the use of diuretics and their effects in babies who have suffered a PH. Restricted fluid intake

has been shown in a Cochrane review [22] to reduce the risks of patent ductus arteriosus. This may indirectly improve the situation during PH. A general approach of fluid overload avoidance would be wise in such cases. Further assessment of the presence of a PDA and its subsequent management would be required.

Coagulopathy

The role of coagulopathy in babies who develop PH is not clear. PH is rarely seen in babies with disseminated intravascular coagulopathy (DIC), thrombocytopenia, haemorrhagic disease of the newborn or haemophilia [23]. However, secondary DIC may occur after a massive PH. If clotting parameters are found to be deranged, fresh frozen plasma can be used for volume replacement.

Other interventions

Administration of endotracheal adrenaline has been in used in PH [24], most often with a dose of 0.1ml/kg (of 1 in 10,000 dilution). This treatment may be considered, but is controversial because there are no controlled trials which have shown a benefit (6).

Tranexamic acid
Mechanism: Tranexamic acid is an antifibrinolytic and acts to prevent clot degradation.

- Dose: 10mg / kg iv 2-3 times daily (this dose is not in any of the usual paediatric dosing literature but has been extrapolated from the paediatric dosing). This treatment may be consider on Consultant discretion.
- Cautions Reduce dose in renal impairment

Long-term complications

Mortality in babies who develop massive PH is high (approximately 50%), especially in those of lower birth weight and gestational age. There seems to be an increased risk of pulmonary or neurodevelopmental complications but this did not reach statistically significant levels [25]. It is difficult to ascertain whether PH itself causes a poor outcome or whether it is a marker for poor outcome in very low birth weight infants who are treated with surfactant [26].

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
A Consultant Neonatologist will be consulted at the time a PH is suspected or being treated (100%)				
All infants that have a PH will have appropriate ventilatory management (100%)				

5. Supporting References

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6. Key Words

Endotracheal adrenaline, Haemorrhagic fluid, High Frequency Oscillatory Ventilation, Surfactant, Tranexamic acid

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS			
Author: Dr. Mark Attard, Dr Sumit Mittal Guideline Lead (Name and Title)			**Executive Lead** Chief medical officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
April 2011	**1**		Original guideline ratified

April 2016	**2**	Guidelines lead (REM) Neonatal Guidelines Meeting Neonatal Governance Meeting	no significant changes (ratified for 1 year) – pending further review
July 2017	**3**	Guidelines lead (REM) Neonatal Guidelines Meeting Neonatal Governance Meeting	
July 2020	**4**	Neonatal Guidelines Meeting Neonatal Governance Meeting	
October 2023	**5**	Neonatal Guidelines Meeting Neonatal Governance Meeting	Background updated Tranexamic acid added to other interventions Updated management flow chart to incorporate changes and, haematology considerations moved to separate box in flow chart.

Appendix 1

Management of PH in a Neonate

Assess the clinical condition of the baby

Nontraumatic gush of bloody secretion from the endotracheal tube, which was associated
With:-
Features suggestive of shock
Clinical deterioration or a need of increased ventilator support

Investigations

FBC
Cross matching
Coagulation profile
Sepsis screening
Blood gas
CXR
CrUSS
2D ECHO-PDA assessment and LV function

Management

Resuscitate: ABC
Inform consultant Neonatologist if you are suspecting or treating PH
Suction airway as required
Surfactant administration (100mg/kg)
Ventilation:
HFOV
Increasing MAP with conventional ventilation[high PEEP(6-8cm of H2O) &high PIP]
May need sedation and skeletal muscle relaxation
Treat haemodynamic instability(consider ionotropes)
Consider correcting coagulopathies
Appropriate fluid management
Treat sepsis
Discuss with consultant

According to the British Society of Haematology guidelines in preterm infants[27,28,29,30] :-
Hb>120g/l(if requiring ventilator support or actively bleeding
Platelets >50
May consider FFP (for abnormal coagulation profile with hypovolemia)
Vit K if PT is elevated
Fibrinogen >1.0g/dl