Pulmonary haemorrhage in the neonate

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Abstract
Pulmonary haemorrhage (PH) in a sick neonate is a life-threatening complication and is often associated with a high mortality. It is now often seen in extreme preterm and very low birth weight infants who are growth restricted and have received surfactant with significant respiratory distress syndrome. The mainstay of treatment includes ventilation and vigorous resuscitation of a shocked and critically ill infant. This review aims to give an overview of the pathogenesis, aetiology and management of PH in a neonate.

Keywords low birth weight; pulmonary haemorrhage; surfactant

Introduction
Pulmonary haemorrhage (PH) is an acute, catastrophic event characterized by discharge of bloody fluid from the upper respiratory tract or the endotracheal tube (ETT). It is a form of fulminant lung oedema with leakage of red blood cells and capillary filtrate into the lungs. It commonly occurs in babies weighing less than 1500 g, who often have a patent ductus arteriosus (PDA), have been treated with surfactant and are ventilated.

Incidence
The incidence of PH in infants with a birth weight less than 1500 g and treated with surfactant was reported to be 11.9%.1

Pathogenesis
PH must be clearly differentiated from the common occurrence of a small amount of blood-stained material aspirated from the ETT of a ventilated baby as a result of trauma. The antecedents of PH are mostly conditions associated with hypoxia or pulmonary oedema in which an acute rise in lung capillary pressure can be expected. The most likely explanation is that massive PH represents the build-up of the capillary filtrate in the pulmonary interstitial space. It bursts through the pulmonary epithelium into the air spaces. There is an association between PH and significant left-to-right ductal shunting and resultant high pulmonary blood flow.2

Aetiology
Massive PH represents the extreme end of the spectrum of pulmonary oedema in the neonate. This has four main causes (Table 1). The risk factors for pulmonary haemorrhage include:
- intrauterine growth restriction
- surfactant therapy
- PDA
- coagulopathy.

Surfactant therapy
PH is thought to occur as a complication of exogenous surfactant therapy but the exact mechanism is not clear. It is thought that surfactant therapy, by increasing pulmonary blood flow as PaO₂ increases, with reduction in pulmonary vascular resistance as the lung function improves, worsens any existing pulmonary oedema and leads to PH. A Cochrane systematic review of seven RCTs in a total of 1583 premature infants concluded that prophylactic treatment with synthetic surfactant increased the risk of PH, meta-analysis showing a RR of 3.28 (95% CI 1.50–7.16).4 In a case-control study of 787 very low birth weight infants treated with surfactant, 11.9% developed PH. In these infants, this was associated with increased risk of death (OR 7.8, 95% CI 2.6–28) and short-term morbidity if moderate or severe.1 In a similar case-control study of 1011 very low birth weight infants, 5.7% developed PH with a mortality of 50%.5 Significantly more infants who developed PH had received surfactant therapy compared with matched controls, despite a similar severity of lung disease. Meta-analysis of 29 trials demonstrated an association of PH with synthetic, but not natural, surfactant use.6 The risk of PH associated with prophylactic and rescue surfactant therapy has been addressed in two Cochrane reviews. Rescue surfactant therapy was not demonstrated to have a significant effect on PH,7 but prophylactic surfactant increased the risk (RR 3.28; 95% CI 1.5–9.2).8

Patent ductus arteriosus
Preterm infants with echocardiographic evidence of a large left-to-right shunt across a PDA and a high pulmonary blood flow have a high incidence of PH.2 In addition, the neonate with severe respiratory distress syndrome (RDS) on intermittent positive pressure ventilation (IPPV) in a high oxygen concentration and with heart failure secondary to a large pulmonary blood flow from a PDA may suffer a PH.

Intrauterine growth restriction
Infants who are small for gestational age are more likely to suffer a PH, the association being independent of other factors.8

Coagulopathy
PH is rarely seen in babies with disseminated intravascular coagulation (DIC), but does not usually occur in babies with thrombocytopenia, haemorrhagic disease of the newborn or haemophilia. However, it is not uncommon for secondary DIC to occur following a massive PH.

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Clinical features

PH commonly occurs between the second and fourth day of life. Clinically, the onset of massive PH is heralded by sudden deterioration of the infant with pallor, cyanosis, bradycardia or apnoea. Pink or red frothy liquid drains from the mouth or can be suctioned through an ETT. The baby usually is hypotensive and is frequently limp and unresponsive, although term babies may occasionally be active and restless secondary to hypoxae mia and fight the ventilator. Occasionally collapse antedates the overt haemorrhage by an hour or two and rarely the baby looks surprisingly well despite the production of copious blood-stained pulmonary oedema. As the condition is commonly secondary to heart failure, the infant may have a tachycardia and the murmur of a PDA is frequently heard. Other signs include hepatospleno megaly, peripheral oedema and a triple rhythm. Auscultation of the chest reveals widespread crepitations with reduction in air entry.

Investigations

Haematological: although the haematocrit of the oedema fluid is usually less than 10%, considerable quantities of blood can be lost and the baby can become severely anaemic. Secondary DIC can develop.

Biochemical: infants with PH usually have the same problems as those with severe RDS, namely hypoglycaemia, hypocalcaemia, hypoalbuminaemia and renal failure, and these should be sought and remedied.

Chest X-ray: infants with a massive PH show a virtual ‘white out’ with just an air bronchogram visible (Figure 1). As the condition improves with IPPV, the changes may clear or merge into those of bronchopulmonary dysplasia (BPD). Rarely, a lobar pattern of consolidation is found, suggesting that the haemorrhage has just occurred in a part of the lung.

Blood gases: all components of the blood gas deteriorate rapidly with severe hypoxia, hypercarbia and metabolic acidosis.

Septic screen: the possibility of infection should be considered and the infant should have a blood culture taken and be commenced on antibiotics.
Treatment

Resuscitation
Initial resuscitation is the priority. The airway should be cleared with suction, and the infant should be intubated and ventilated and/or the ventilator pressures increased. The circulatory volume should be restored with boluses of colloid 20 ml/kg, a combination of fresh frozen plasma, blood and platelets, with regular re-assessment.

Ventilation
All babies with massive PH should be intubated and ventilated. They usually have severe lung disease, and a peak inflating pressure above 30 cm H2O may be required. A ventilation strategy of high positive end-expiratory pressure (PEEP) (up to 6–7 cm H2O) is used with a long inspiratory time (0.4–0.5 s). Although high positive end-expiratory pressure may be required to keep the ETT clear.

Paradoxically, although surfactant may precipitate PH, after stabilization and ventilation–perfusion balance. Frequent suctioning may be required to keep the ETT clear.

Surfactant
Paradoxically, although surfactant may precipitate PH, after stabilizing the baby on the ventilator, a single dose of surfactant has been suggested to improve oxygenation.10

Circulation
Once the initial circulating volume is restored, the infant needs re-assessing for signs of cardiac failure and pulmonary oedema. Intermittent colloid infusions and inotropes are often required to maintain the blood pressure and cardiac contractility. Blood transfusions may be required to correct anaemia and fresh frozen plasma for clotting derangements. Diuretics may be required if there is significant fluid overload.

Antibiotics
Sepsis is a recognized cause of PH, thus broad-spectrum antibiotics should be started after taking cultures.

Complications
These babies are susceptible to all the major complications of respiratory failure. High pressure ventilation predisposes to air leaks and BPD is a common sequelae. At the time of collapse they are susceptible to neurological damage and major intraventricular haemorrhage (OR 3.1; CI 1.5–6.4 in surfactant-treated very low birth weight infants). However, survivors who could be assessed at 2 years did not differ significantly in neurodevelopmental outcomes when compared to controls.

Mortality
In the modern era of intensive care, survival is improved; but affected infants are the sickest and most immature and their mortality rate is of the order of 38%.11

REFERENCES

FURTHER READING

Practice points
• PH remains a catastrophic complication in an already sick, ventilated preterm neonate
• It should be distinguished from the common occurrence of a small amount of traumatic bleeding aspirated from the ETT
• Risk factors for developing PH are extreme prematurity, growth restriction, surfactant therapy and PDA
• The mainstay of treatment includes ventilation and vigorous resuscitation of a shocked and a critically ill infant