PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN (PPHN)

RECOGNITION AND ASSESSMENT

Definition

- Failure of normal postnatal fall in pulmonary vascular resistance
- Leads to right-to-left shunting and subsequent hypoxia
- Can be primary (idiopathic) or secondary
- Severe hypoxaemia (PaO_2 <6 kPa) in 100% oxygen
- Complex condition with varied causes and degrees of severity
- Echocardiogram: structurally normal heart (may show right ventricular hypertrophy), right-to-left or bidirectional shunt at PFO and/or patent ductus arteriosus (PDA)

Idiopathic

- Degree of hypoxia disproportionate to degree of hypercarbia
- Mild lung disease (in primary/idiopathic PPHN)

Secondary:

- May be associated with
- severe lung disease [e.g. meconium aspiration (MAS), surfactant deficiency]
- perinatal asphyxia
- infection [e.g. Group B streptococcal (GBS) pneumonia]
- structural abnormalities: pulmonary hypoplasia, congenital diaphragmatic hernia, A-V malformations, congenital cystic adenomatoid malformation (CCAM)
- maternal drugs: aspirin, non-steroidal anti-inflammatory drugs, SSRIs

CLINICAL FEATURES

Usually present in first 12 hr of life

- SpO_2 <95% or hypoxia (PaO_2 <6 kPa) in 100% oxygen
- Mimics cyanotic heart disease
- CVS: tricuspid regurgitant murmur, right ventricular heave, loud second heart sound and systemic hypotension
- Idiopathic PPHN: respiratory signs mild or absent
- Secondary PPHN: features of underlying disease

INVESTIGATIONS

- Blood gas shows hypoxaemia (PaO_2 <6 kPa) with oxygenation index >20 (underlying disease will produce a mixed picture)
- SpO_2 >5% difference in preductal (right hand) and postductal saturations (either feet) (pre > post)
- Hyperoxia test (100% oxygen for 5 min)
- SpO_2 may improve to ≥95% in early stage **or** may not respond, i.e. staying <95% in established PPHN (as in cyanotic heart disease)
- Chest X-ray: variable findings depending on underling diagnosis (normal or minimal changes in idiopathic PPHN)
- Electrocardiograph – often normal. Can sometimes show tall P waves in lead 2/V1/V2 or features of RVH (i.e. tall R waves V1/V2, right axis deviation or upright T waves in V1/V2)
- Echocardiogram (although not mandatory for initial diagnosis and management) is useful:
- to exclude cyanotic heart disease
- to assess pulmonary pressure
- to evaluate ventricular function
- ≥1 of the following confirm PPHN in presence of normal cardiac structures:
  - significant tricuspid regurgitation
  - dilatation of right side of heart and/or hypertrophy of right ventricle
  - right-to-left shunting across PFO and/or PDA
  - pulmonary regurgitation

  - flattening or bowing of interventricular septum towards right ventricle
- Pulmonary pressure is estimated from echocardiogram using either:

  Tricuspid regurgitation (systolic pulmonary pressure = $4 \times (\text{VmaxTR})^2$ + usual right atrial pressure of 5)

  Pulmonary Regurgitation (mean pulmonary pressure = $4 \times (\text{VmaxPR})^2$ + usual right ventricular diastolic pressure of 5)

MANAGEMENT

- If saturations continue at <95% despite 100% oxygen, and echocardiography not available immediately to rule out duct dependent heart disease, start prostaglandin infusion IV
- Once PPHN suspected, inform and involve consultant neonatologist immediately
- Aims of management are to:
- decrease pulmonary vascular resistance
- increase systemic blood pressure
- treat any underlying condition

General measures

- Minimal handling, nurse in quiet environment
- Secure arterial and central venous access, see **Arterial line insertion** guideline or **Umbilical artery catheterisation and removal,** and **Umbilical venous catheterisation and removal** guidelines
- Maintain normal temperature, biochemistry and fluid balance
- Keep Hb ≥120 g/L
- Give antibiotics (sepsis, particularly GBS, is difficult to exclude)
- Surfactant may be beneficial in MAS or GBS sepsis – discuss with consultant
- If perfusion poor, fluid bolus [sodium chloride 0.9% 10 mL/kg or if coagulopathy, fresh frozen plasma (see **Coagulopathy** guideline)]
- Once $PaCO_2$ in acceptable range (i.e. <6 kPa), correct metabolic acidosis to maintain pH 7.35–7.45 using full correction with sodium bicarbonate over 1 hr. If repeat correction necessary, **slow** bicarbonate infusion of calculated dose can be given over 6–12 hr (see **Neonatal Formulary**)

Ventilation

- Use conventional ventilation to start with (targeted tidal volume 5–6 mL/kg)
- Use sedation and muscle relaxation in babies with high ventilatory and oxygen requirements and/or ventilator asynchrony
- $PaCO_2$ 4.5–5.5 kPa (accept up to 6 kPa in parenchymal lung disease). Avoid hypocarbia
- start in 100% oxygen and reduce as tolerated. Maintain SpO_2 at 96–100% and PaO_2 at 10–12 kPa
- High frequency oscillatory ventilation (HFOV) may further improve oxygenation [see **Ventilation: high frequency oscillatory ventilation (HFOV)** guideline]
- Monitor oxygenation index (OI)

$$\text{OI} = \frac{\text{mean airway pressure (cm } H_2O) \times \text{\% of oxygen}}{\text{postductal } PaO_2 \text{ (kPa)} \times 7.5}$$

Inotropes (**see *Hypotension* guideline)**

- Use inotropes early
- In significant PPHN, adrenaline or noradrenaline can be useful in increasing systemic blood pressure without increasing pulmonary vascular resistance
- Maintain systemic mean BP 50–60 mmHg in term baby and systemic systolic BP 60–70 mmHg or above estimated pulmonary pressures (if available by echo)

Pulmonary vasodilatation

- If OI >20 or needs 100% oxygen, or significant PPHN on echo, use inhaled nitric oxide (NO) as a selective pulmonary vasodilator (see **Nitric oxide** guideline)
- Babies with PPHN requiring NO should be referred to a NICU for ongoing management

Severe and resistant PPHN not responding to conventional management

Baby born ≥34 weeks or ≥2 kg with PPHN

- Not responding or OI >30 despite NO, inotropes and/or HFOV **or**
- Unable to maintain BP with inotropes or persistent need for adrenaline/noradrenaline infusion **or**
- No significant progression after 3 days
- May benefit from ECMO or other specialist treatment
- Discuss with KIDS team in West Midlands or nearest ECMO centre
- Liaise with PICU/ECMO team regarding other medical management

Criteria for ECMO

- Baby born ≥34 weeks or ≥2 kg with PPHN
- Oxygenation index >40
- Reversible lung disease (<10 days high pressure ventilation)
- No lethal congenital malformation

Exclusion criteria (if in doubt, discuss with ECMO team)

- Major intracranial haemorrhage
- Irreversible lung injury or mechanical ventilation >10 days
- Lethal congenital or chromosomal anomalies
- Severe encephalopathy
- Major cardiac malformation

A baby accepted for transfer to ECMO centre will be retrieved by ECMO or PICU team

- ECMO centre will need:
- cranial ultrasound scan
- maternal blood for group and crossmatching (check with ECMO centre)
- referral letter
- copies of hospital notes/chest X-rays
- Outreach ECMO
- ECMO team may decide to start outreach ECMO in NNU before transfer to ECMO unit. Check with ECMO team regarding diathermy unit and number of packed cell units needed for procedure

Referral for ECMO

- For West Midlands contact KIDS team on 0300 200 1100, or
- ECMO co-ordinator/fellow at nearest ECMO centre:
- Glenfield Hospital, Leicester 0116 287 1471
- Great Ormond Street Hospital, London 0207 829 8652
- Freeman Hospital, Newcastle 0191 223 1016
- Yorkhill Hospital, Glasgow 0141 201 0000