NTS Clinical Guideline

Title:	Persistent Pulmonary Hypertension of the Newborn (PPHN)		
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Definition

Persistent Pulmonary Hypertension (PPHN) of the newborn is defined as delay in the normal postnatal decline in pulmonary vascular resistance resulting in arterial hypoxemia, with associated shunting of de-oxygenated blood across to the systemic circulation resulting in persistence of the foetal circulation.

Three main types:

1. PPHN with initially normal lungs e.g. perinatal asphyxia, sepsis, congenital heart disease, maternal diabetes, Down's Syndrome

2. PPHN associated with hypoplasia of lung tissue e.g. congenital diaphragmatic hernia, Potter's syndrome, oligohydramnios

3. PPHN associated with pulmonary parenchymal disease or primary pulmonary hypertension e.g. respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), chronic fetal hypoxia with increased smooth muscle, pneumonia

Pulmonary hypertension may also present in preterm babies following an acute deterioration. Although this pathology is different to PPHN, the approach to management is similar. Use of inhaled nitric oxide in preterm babies is controversial.

Recognition

- Usually presents in term or post-term infants
- Onset at birth or a few hours after birth
- May be an insidious onset in babies who have experienced borderline oxygenation for several hours without respiratory support or with non-invasive ventilation

Signs

- Cyanosis
- Tachypnoea
- Low arterial pO2 levels - presentation often mimics cyanotic congenital heart defect
- pCO_2 normal or low (unless there is also parenchymal lung disease)
- Chest x-ray may be normal
- Evidence of right to left shunt may be present with difference in pre- and post-ductal SpO_2, swinging SpO2 or PaO2

Management approach

	Investigations, Stabilization and Management

Airway	• Chest X ray
	  ○ To confirm the position of the ET tube (T1-2)
	  ○ Rule out pneumothorax and
	  ○ Check for lung pathology and lung expansion
	• Upsize the ET tube if there's a leak
	• Suction the airway to clear secretions
	• Decompress the stomach with NG tube

Breathing	• Monitor pre and post ductal saturation differences (normality <5%) • Monitor the arterial blood gas • Aim for pH 7.30-7.40, pCO2 4.5-5kPA, pO2 10-15kPA • Calculate OI regularly (Refer to Appendix 2) • Involve ECMO team if OI is trending upwards beyond 30 for early advice and referral • Optimise lung recruitment by altering: mean airway pressure, Ti and rate • Oscillation may be helpful depending on the lung pathology and optimise altering MAP, Amplitude and frequency. • In Meconium Aspiration – suctioning and chest physiotherapy and consider surfactant administration at 200mg/Kg • Give FiO2 100% and do not try to wean during stabilisation • Use of iNO at 20ppm if oxygenation continues to be suboptimal. • Use adequate analgesia and sedation • Use muscle relaxation if synchrony and gas exchange continue to be a problem
Circulation	• Monitor arterial BP, aim for mean ABP 50-60 (may need higher if the pulmonary pressures are high) • If possible, echo to rule out cyanotic CHD, confirm right to left shunting and effective myocardial contractility • Correct acidosis • Optimise intravascular volume • Consider blood products as necessary • Central venous access for inotropes • Consider the most appropriate inotrope early (as it may take time to get these prescribed and available) based on clinical assessment (Refer to Appendix 1) • If there's a need to add more than two inotropes, consider Hydrocortisone IV bolus (2.5mg/Kg)
Disability	• Monitor blood glucose aim > 3 mmol/L • Monitor and optimise electrolytes: ionized calcium (≥ 1mmol/L), Magnesium (≥ 0.7 mmol/L) • Cranial US to rule out intracranial bleeding • Optimise sedation
Everything else	• Normal temperature, avoid hypothermia • Update parents, NTS Consultant and Receiving unit (they need to know the infusions and use of iNO in advance so that these are set up and ready before you arrive) • Ideally such cases should be discussed using three way Conference call.

Consideration for ECMO

ECMO for term babies with severe hypoxic respiratory failure has been shown to improve survival significantly, without increasing the risk of long-term neurodevelopmental deficit[1]. Where conventional therapy is failing, discussion with an ECMO centre should take place as soon as possible.

Indications for ECMO referral[2]

- Oxygenation Index > 25
- Weight >2kg
- Gestation > 35 weeks
- Severe but reversible cardiac or pulmonary disease unresponsive to optimal ventilation and pharmacological therapy

Contraindications for ECMO include

- Major intracranial haemorrhage (> Grade 2 IVH)
- Prolonged asphyxia predicted to cause brain damage or other irreversible organ dysfunction
- Lethal congenital abnormality

Referral for ECMO

Within London, referrals should be made to Great Ormond Street Hospital via the CATS team on 0207 430 5850 who will be able to offer an ECMO cot or negotiate referral to another regional team.

Following discussion with the ECMO team, it can be decided whether the NTS team or the CATS team would be most appropriate to expedite the transfer. The main considerations should be optimisation of treatment and timely movement of the baby before further deterioration occurs.

Counselling of Parents

PPHN is associated with a mortality rate of up to 10%, but may be greater if there is an underlying congenital disorder[3]. It is associated with neurodevelopmental deficit including cerebral palsy and hearing loss[4] but it is impossible at the outset to predict the course of the disease.

Parents must be aware that their baby is very sick and if there is doubt about the likelihood of surviving the transfer or early management at the accepting unit then this must be clearly communicated. The risk of long-term neurodevelopmental problems should be broached if appropriate.

References

[1] Mugford M, Elbourne D, Field D. Extracorporeal membrane oxygenation for severe respiratory failure in newborn infants. Cochrane Database Syst Rev. 2008 Jul 16;(3):CD001340. doi: 10.1002/14651858.CD001340.pub2.
[2] Children's Acute Transport Service. Extracorporeal Membrane Oxygenation (ECMO) Referrals. http://site.cats.nhs.uk/wp-content/uploads/2013/12/cats_ecmo_2013.pdf
[3] Bendapudi P, Rao GG, Greenough A. Diagnosis and management of persistent pulmonary hypertension of the newborn. Paediatr Respir Rev. 2015 Jun;16(3):157-61. doi: 10.1016/j.prrv.2015.02.001
[4] Konduri GG, Vohr B, Robertson C, et al. Early Inhaled Nitric Oxide Therapy for Term and Near Term Newborn Infants with Hypoxic Respiratory Failure: Neurodevelopmental Follow-Up. The Journal of pediatrics. 2007;150(3):235-240.e1. doi:10.1016/j.jpeds.2006.11.06.

Appendix 1: Inotropes

Assessment / Inotrope	Poor contractility	Peripherally vasodilated "warm shock"	Peripherally vasoconstricted "shut down" / "cool shock"	Tachycardia
Dopamine 5-10 mcg/kg/min	✓		✓	✗
Dopamine 10-20 mcg/kg/min	✓	✓	✗	
Noradrenaline 0.1-1.0 mcg/kg/min		✓ ✓	✗ ✗	
Dobutamine 5-20 mcg/kg/min	✓ ✓	✗ ✗	✗	✗ ✗
Adrenaline 0.03-0.1 mcg/kg/min	✓	✗	✓	
Adrenaline 0.1-1.0 mcg/kg/min		✓	✗	✗

✓ - likely to be useful ✓✓ - very likely to be useful

✗ - risk of worsening picture ✗ ✗ - likely to worsen picture

Appendix 2: Calculation of Oxygenation Index

$$OI = \frac{F_iO_2 \times MAP(cmH_2O) \times 100\%}{P_aO_2(mmHg)}$$

UK gas machines usually give PaO2 in kPa so to convert PaO2 (mmHg) = PaO2 (kPa) x 7.5

Ideally MAP should be a measured parameter from a modern ventilator. If using a more basic device it may be calculated as follows:

$$M_{PAW} = MAP\ (cmH_2O) = \frac{(PIP\ \times T_i) + (PEEP \times T_e)}{T_i + T_e}$$

Where PIP = Peak inspiratory pressure cmH2O
PEEP = Positive end expiratory pressure cmH2O
Ti = Inspiratory time s
Te = Expiratory time s