NETS WA
Newborn Emergency Transport Service

Persistent Pulmonary Hypertension of the Newborn (PPHN)

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

Aim

To provide information to the NETS WA retrieval team on management of a neonate with PPHN.

Risk

Delayed recognition and suboptimal management of PPHN may lead to failure to establish adequate ventilation and oxygenation.

Definition

Persistent Pulmonary Hypertension of the Newborn (PPHN) is a complex condition with inappropriate resistance to blood flow through the pulmonary vascular bed resulting in Hypoxic Respiratory Failure. It may present with failure of circulatory adaptation following the birth or secondary to lung dysfunction which should be promptly identified and treated where possible.

Key Points

- PPHN should be considered in any infant with marked hypoxemia, especially in late preterm, term and growth-restricted infants.
- PPHN can mimic congenital cyanotic heart diseases or can be an accompanying feature of cyanotic heart disease.
- The maternal, neonatal, and perinatal conditions that are associated with PPHN in neonates are maternal hyperglycaemia, maternal use of NSAIDs and SSRIs, caesarean section, chorioamnionitis, Down syndrome, Arterio-Venous Malformation

(Vein of Galen), hypocalcaemia, and neonates with hypoxic ischaemic encephalopathy.

- When PPHN is suspected (and/or iNO is required for management), the on-call NETS consultant MUST be notified.
- Clinical conditions where iNO is of benefit are; Meconium Aspiration Syndrome, severe Hyaline Membrane Disease, congenital pneumonia, congenital respiratory malformations, and diaphragmatic hernia.
- iNO is effective in term and near-term infants with hypoxic respiratory failure and reduces the incidence of death or use of ECMO (Extracorporeal Membrane Oxygenation). The use of iNO in premature babies MUST be considered under the guidance of the NETS Consultant.

Diagnostic clues

- **Clinical presentation:** Infants with PPHN may have a prominent precordial impulse, a loud second heart sound, or a systolic parasternal murmur due to tricuspid incompetence. May also present with differential cyanosis between the upper and lower limbs.
- **Cardiopulmonary monitoring:** Pre- and post-ductal SpO2 difference > 5-10% might be expected.
- **Blood gas:** May be pO2 differentiation between upper and lower limbs. The degree of hypoxia is variable and the pCO2 may be normal or low.
- **Chest x-ray:** In Primary PPHN the lung fields are often clear or minimally opacified on x-ray, whereas in secondary PPHN the Chest x-ray is mostly abnormal, in keeping with the underlying respiratory condition (e.g., ground glass appearance in respiratory distress syndrome and patchy infiltration in Meconium Aspiration Syndrome). In both types of PPHN large cardiac shadow can be detected on chest x-ray.

Management

During retrieval planning of babies with suspected PPHN, take a retrieval cot with inhaled nitric oxide. For metropolitan retrievals, there is also the option to take the Fabian transport ventilator (High-frequency Oscillation Ventilation).

1. **Optimise ventilation**
   - Intubation and mechanical ventilation, with premedication (sedation, muscle relaxant and judicious use of Atropine), while aiming for PH near 7.4, PcO2 35-45 mmHg, SpO2 94-97%, and PaO2 60-90 mmHg are the main steps of respiratory management.
   - FiO2 should be weaned slowly as sudden changes in FiO2 will create hypoxemic episodes which can worsen PVR (Pulmonary Vascular Resistance). Conventional mechanical ventilation (CMV) using a patient-triggered volume-targeted mode is the first option for most neonates.

- For infants requiring peak pressures on CMV that are ≥28 to 30 cm H2O and those who develop significant air leaks on CMV, transitioning to high-frequency ventilation (HFV) should be considered.

2. **Administer surfactant**
   - Early surfactant administration may be beneficial where PPHN is secondary to parenchymal lung disease (e.g., Meconium Aspiration Syndrome) or secondary to surfactant deficiency (e.g., pneumonia and sepsis).
   - Overall systemic stability should be considered when contemplating surfactant and a small volume drug r.g. Poractant Alpha should be the first choice.

3. **Place a central line**
   - Placing both umbilical venous and arterial catheters is recommended but MUST be discussed with the on-call NETS Consultant.
   - If a short journey is expected, central access can be considered on arrival in the destination unit.

4. **Maintain normothermia and euvolemia (Using Saline bolus & Inotropes)**
   - Optimal preload is crucial in maintaining cardiac output in the newborn. Volume expansion with saline boluses (or blood if indicated) should be considered and mean arterial pressure (MAP) should be maintained above 50 mmHg.
   - The use of inotropes in the management of PPHN is always a double-edged sword. The choice of inotropes MUST be discussed with the on-call NETS consultant.

5. **Correct metabolic acidosis, and electrolyte imbalance, and maintain euglycemia:**
   - Aim for a pH of around 7.40. Serum Electrolyte levels (Na, K, Ca, and Mg) should be measured and corrected.
   - Consider bicarb infusion if there is resistant acidosis (pH is less than 7.00 despite optimal ventilatory and inotropic management).

6. **Reduce discomfort (analgesia and sedation)**
   - Avoid excessive handling and sedate adequately. Fentanyl is a good first-line drug as it is more potent than Morphine.
   - Position/nest the infant appropriately and minimize tactile stimulation and loud talking. Most babies with PPHN are kept Nil by mouth, however, they can receive mouthcare with breastmilk on a cotton swab. Some may still require muscle relaxation (e.g. Vecuronium) after discussion with the on-call NETS consultant.

7. **Avoid anaemia/polycythaemia**
   - Hb should be sufficient to provide adequately oxygenate. Aim to maintain haemoglobin >100 g/L.

8. **Treat sepsis with antibiotics**

9. **Consider pulmonary vasodilators**
   - Pulmonary vasodilators aim to decrease the abnormally elevated pulmonary vascular resistance by relaxing vascular smooth muscle within the pulmonary circuit and increase systemic vascular resistance when it is inadequate.
   - Pulmonary vasodilators may cause systemic hypotension.

Refer to the ready reckoner list before leaving the referring site to ensure all steps have been followed.

Inhalation Nitric oxide (iNO):

- iNO is the first line of treatment in PPHN. Consideration of using iNO during retrieval requires greater clinical judgment as to the possible underlying causes for hypoxia, since investigations such as echocardiogram and pre and post-ductal oxygen saturation measurements may not be available.
- Consequently, a 'trial of therapy' may be indicated on the grounds of the clinical history and examination findings alone.
- The use of inhaled nitric oxide on non-invasive ventilatory devices is not recommended. iNO should be used when the baby has been intubated and ventilated.
- An Echocardiography is not required for initiating iNO. Oxygenation Index (OI) >25 or >15 in the presence of very rapid deterioration is another indicating parameter for starting iNO. (Please refer to Appendix for OI calculation)
- Ensure lungs are adequately inflated while considering NO.

1. **Indications:**
   - iNO is indicated in infants with hypoxic respiratory failure.
   - Clinical evidence of pulmonary hypertension:
     - SpO2 <85% despite FiO2 >80%.
     - Pre- and post-ductal SpO2 difference >10%.
     - Hypoxia despite high ventilation settings (e.g., Fio2 >40%, PIP > 30 cmH2O etc).

2. **Relative Contraindications:**
   - Coagulopathy, active bleeding, stage 3 HIE, lethal congenital malformation, and imminent death.
   - Complications should be considered in the context of retrieving a baby for definitive care and the risk/benefit of iNO treatment.
   - Although evidence is not robust for the use of iNO in some circumstances its use as a temporary measure is acceptable until definite treatment or decisions on the direction of therapy can be made.

3. **Dosage, response, and maintenance:**
   - Term Infants (≥ 37w): Commence iNO at 10-20ppm. Doses more than 40 ppm are not recommended and are rarely effective if there is no response to the original dose.
   - Preterm Infants (< 37w): Commence iNO at 5-10ppm. Doses above 20 ppm are not recommended.
   - Repeat blood gas 30 minutes after commencement.
   - Close observation of haemodynamic changes, FiO2 requirement, and pre/post ductal SpO2 is recommended in addition to lung volume assessment by chest-x ray to optimise oxygenation and avoid excessive ventilation (PCO2 <40).
   - As a rule, iNO commenced during transport should be continued at the effective dose (and not weaned) until return to the accepting hospital.

4. **Potential complications:**
   - Although there is a small potential risk of intoxication while an entire NO cylinder gets discharged, there is excellent evidence to show that the complete discharge of a NO cylinder in a well-ventilated enclosed space (such as in an aircraft or ambulance), does not result in dangerous levels of either NO or NO_2 due to the usual turnover of air in transport vehicles or aircraft.
   - Some of the complications of iNO exposure are as follows;
     - Eyes: iNO is corrosive to the eyes and is most dangerous for those wearing contact lenses. Wearing protective goggles is highly recommended in close proximity to the iNO cylinders. Removal of contact lens and immediately flush with large volumes of tepid water or saline for 15-20 minutes should be attempted when eyes are exposed to iNO.
     - Inhalation: Immediate inhalation will cause irritation to the nose and throat.
     - Suggested late effects (up to 72 hours): Cough, chest pain, nausea, dyspnoea, and haemoptysis (Note: none of these side effects has been noted in any trials of iNO).

Related CAHS internal policies, procedures and guidelines

NETS Transport Medications

- https://www.cahs.health.wa.gov.au/~/media/HSPs/CAHS/Documents/Health-Professionals/NETS/Transport-Medications.pdf
- Child and Adolescent Health Service | CAHS - NETS WA clinical guidelines and protocols

Neonatology Guidelines

- Persistent Pulmonary Hypertension of the Newborn (health.wa.gov.au)

References and related external legislation, policies, and guidelines

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20-Neonatal handbook, Christ church hospital, 2017
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22-PPHN guideline, Royal Prince Alfred Hospital, NSW, 2014

This document can be made available in alternative formats on request

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Appendix

OI calculation

- The severity of PPHN is commonly assessed by oxygenation index (OI) reflecting the efficiency of oxygen uptake.
- This index calculation includes MAP (mean airway pressure in cmH2O), FiO2 (fraction of inspired oxygen), and PaO2 (partial pressure of oxygen in arterial blood (in mmHg).
- Based on OI, hypoxemic respiratory failure can be classified into mild (OI ≤ 15), moderate (OI > 15 to 25), severe (OI 25 to 40), and very severe (OI > 40).
- Oxygenation Index (OI): $OI = \frac{FiO2 \times MAP \times 100}{PaO2}$

Ready reckoner list

It is recommended to go through the ready reckoner list before leaving the referring site to ensure all steps have been followed.

1. Ready reckoner list
2. Optimal airway ensured (ETT)
3. Optimal ventilation achieved (PC-AC/HFOV +/- surfactant)
4. Optimal oxygenation achieved (appropriate Mean airway pressure, inhaled nitric oxide)
5. Optimal IV access (PIVC +/- UVC/UAC/PAL)
6. Optimal circulation ensured (IV fluids +/- inotropes +/- steroids)
7. Optimal management of infection (antibiotics administered)
8. Optimal management of coagulopathy (ensure normal platelets, vit K administration, INR normal)
9. Optimal sedation and analgesia ensured (Morphine/Fentanyl +/- vecuronium)
10. Neurodevelopmental care ensured (need for therapeutic hypothermia, minimal handling, ear muffs, eye goggles)
11. Optimal assessment of the lab reports and imaging at referral site
12. Optimal assessment of transport logistics (road/air, distance, travel time)