HEALTH HOLDING

HAFER ALBATIN HEALTH CLUSTER
MATERNITY AND CHILDREN HOSPITAL

Department:	Neonatal Intensive Care Unit (NICU)		
Document:	Departmental Policy and Procedure		
Title:	Management of Persistent Pulmonary Hypertension in Neonates		
Applies To:	All NICU Staff		
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1. PURPOSE:

1.1 Persistent pulmonary hypertension of the newborn (PPHN) is a frequent cause for admission to the neonatal intensive care unit and is associated with mortality and variable morbidities such as chronic pulmonary disease and neurodevelopmental disabilities.

2. DEFINITIONS:

2.1 Pulmonary hypertension (PHT) is a serious cardiopulmonary disorder characterized by elevated mean pulmonary artery pressure (mPAP) and prolonged exposure of the right ventricle to high afterload

2.2 Persistent pulmonary hypertension of the newborn (PPHN) is a syndrome that occurs when the high pulmonary vascular resistance characteristic of fetal circulation fails to decrease at birth, resulting in right-to-left shunting of blood through fetal channels, diminished pulmonary blood flow and profound labile hypoxemia. PPHN can be a primary condition or can be secondary to a variety of disorders.

3. POLICY:

3.1 In the delivery room: Early recognition of PPHN and correction of factors that prevent decrease in PVR (Pulmonary Vascular Resistance) are important for successful management:

- 3.1.1 Suspect PPHN in a hypoxic term or near term neonates with risk factors for PPHN e.g. meconium-stained amniotic fluid, perinatal acidosis and asphyxia prolonged rupture of membranes, maternal fever and positive group B Streptococcal carrier status, chorioamnionitis, medications as non-steroidal anti-inflammatory drugs during late pregnancy, maternal obesity, advanced age, diabetes, birth by cesarean section, large and small for gestational age.
- 3.1.2 Resuscitate according to the steps of NRP.
- 3.1.3 Focus on optimal lung recruitment and ventilation.
- 3.1.4 Maintain pre-ductal SpO2 in the ranges recommended by the NRP. Excessive oxygen during resuscitation results in rapid decrease in PVR but increases subsequent pulmonary arterial contractility and reduces response to inhaled NO.

3.2 In NICU:

- 3.2.1 Diagnosis: Differentiate between PPHN and cyanotic congenital heart disease (CCHD)
  - 3.2.1.1 A single, or narrowly split and accentuated S2 and a systolic murmur of tricuspid regurgitation are often heard in PPHN.
  - 3.2.1.2 Factors which may point towards CCHD include family history, relative absence of signs of respiratory distress, presence of significant murmur, weak lower limb pulsations, and abnormal heart shape on chest radiograph.
  - 3.2.1.3 Labile hypoxemia is one of the classic features of PPHN, unlike fixed hypoxemia seen in CCHD.
  - 3.2.1.4 Simultaneously measure pre- and post-ductal SpO2 and PaO2:
- 3.2.2 SpO_2 differences of greater than 5% to 10% or PaO_2 differences of 10 to 20 mm Hg between right upper limb and lower limbs are considered significant:

3.2.2.1 Upper body greater than lower body:
3.2.2.1.1 PPHN (with PDA),
3.2.2.1.2 Ductal-dependent systemic blood flow lesions (such as hypoplastic left heart syndrome, critical aortic stenosis, interrupted aortic arch, and coarctation of aorta). Treatment strategies aimed to lower PVR in these patients may cause their clinical deterioration.
3.2.2.1.3 Anatomic pulmonary vascular disease (pulmonary venous stenosis, TAPVR, and alveolo-capillary dysplasia/mal alignment of pulmonary veins).
3.2.2.2 No difference between upper and lower saturations:
3.2.2.2.1 Bidirectional ductus arteriosus flow (systemic PVR).
3.2.2.2.2 Closed ductus arteriosus with PPHN and atrial level right-left shunting both the right arm and the leg SpO_2 will be low (also includes premature in utero closure).
3.2.2.2.3 Large intra-cardiac shunt equalizing saturations in right and left ventricles.
3.2.2.2.4 Anomalous take-off of right subclavian artery (post-ductal position).
3.2.2.3 Upper body less than lower body "reverse differential":
3.2.2.3.1 Transposition of the great vessels associated with PPHN or coarctation of aorta.
3.2.2.3.2 Other forms of structural heart disease with preferential streaming of blood flow e.g. TAPVR
3.2.2.3.3 Often due to poor perfusion in the right hand secondary to a peripheral intravenous cannula arm splint.

3.2.3 Chest radiography and blood gases:
3.2.3.1 RDS, MAS, or pneumonia may be seen on chest X-ray in secondary PPHN,
3.2.3.2 Hypoxemia disproportionate to the severity of parenchymal disease on chest X-ray should suggest PPHN (or cyanotic heart disease).
3.2.3.3 Idiopathic or "black-lung" PPHN is not associated with parenchymal lung disease; there is reduced pulmonary blood flow with normally or slightly hyper-inflated lungs.
3.2.3.4 Pulmonary hypoplasia e.g. secondary to oligohydramnios.

3.2.4 CBC with differential evaluates the risk of underlying infection or polycythaemia (increased viscosity) contributing to intrinsic vascular obstruction and PPHN.

3.2.5 Echocardiography is the gold standard to confirm the diagnosis of PPHN, assess right and left ventricular function, monitor the efficacy of specific therapeutic interventions and rule out CCHD.

4. PROCEDURE:

4.1 The severity of PPHN can range from mild hypoxemia with minimal respiratory distress to severe hypoxemia and cardiopulmonary instability that requires intensive care.

4.2 Infants with PPHN require supportive care tailored to the degree of hypoxemia and physiologic instability.

4.3 Early detection, monitoring and management of mild cases:

4.3.1 Caesarean delivery, induction of labor of the late preterm, use of anaesthetics and analgesics delay pulmonary transition at birth, these infants present with "delayed cardiorespiratory adaptation":

4.3.2 Management with appropriate respiratory support to recruit the lungs and provide optimal inflation (while avoiding atelectasis {from very high FiO_2} and hyperinflation) reduce PVR and the risk of PPHN e.g. provide CPAP if FiO2 >30%

4.3.3 Mild cases of PPHN with minimal or no respiratory distress can be detected in the postnatal ward either following a desaturation episode or by low post-ductal oxygen saturation detected on critical congenital heart disease screening:

4.3.4 Manage with supportive care and oxygen supplementation.

4.3.5 Close monitoring is important as some of these infants may rapidly deteriorate and require non-invasive ventilation or intubation and mechanical ventilation.

4.4 Target therapy to the underlying disease e.g.:

4.4.1 Antibiotics for sepsis (elevated pulmonary pressures often associated with systemic hypotension can be the presenting feature of pneumonia or sepsis),

4.4.2 Surfactant for infants with PPHN secondary to parenchymal lung disease such as RDS, pneumonia, sepsis or MAS.

4.5 **Supportive care:**

4.5.1 Maintain normal temperature,

4.5.2 Correct metabolic and hematologic abnormalities such as hypoglycemia, hypocalcaemia, acidosis, polycythaemia.

4.5.3 Judicious use of sedation and analgesia with morphine, fentanyl or midazolam decrease oxygen consumption from agitation in hypoxemic or ventilated patients.

4.5.4 Avoid paralysis if possible, as it has been associated with increased mortality.

4.5.5 Intravenous fluids /TPN preferably through a central line.

4.5.6 Close monitoring of core temperature, systemic and pulmonary hemodynamics and oxygenation during hypothermia therapy and rewarming for HIE patient.

4.6 Maintain pH > 7.25. Preferably 7.30 to 7.40 during the acute phase of PPHN.

4.7 **Ventilation**:

4.7.1 Gentle ventilation with optimal PEEP (4-6 cm H_2O), relatively low PIP (maximum 25-28 cm H_2O), tidal volume (4-6 ml/kg) and a degree of permissive hypercapnia are recommended to ensure adequate lung expansion while limiting barotrauma and volutrauma.

4.7.2 Optimal lung recruitment;

4.7.3 HFOV: If a PIP of greater than 25 to 28 cm H2O or tidal volumes greater than 6ml/kg are required to maintain a $PaCO_2$ less than 60 mm Hg on conventional ventilation, switch to high-frequency ventilation.

4.8 **Oxygen therapy**:

4.8.1 Maintain pre ductal SpO_2 in low to mid 90s with PaO_2: levels between 55 to 80 mmHg

4.8.2 If the serum lactate levels are normal (< 3 mmol/L) and urine output is adequate (> 1 ml/kg per hour), post ductal oxygen saturations in the 70s and 80s would be acceptable especially in infants with CDH (congenital diaphragmatic hernia).

4.9 **Blood pressure**:

4.9.1 Maintain adequate systemic blood pressure at normal values for gestational age and avoid supra-physiological systemic pressure.

4.9.2 Aiming for supra-physiologic blood pressure to reverse/limit the right to left shunting is not recommended. It may improve oxygenation.

4.10 **Inhaled Nitric Oxide (iNO)**:

4.10.1 iNO is a potent and selective pulmonary vasodilator without a significant decrease in systemic blood pressure, and is also preferentially distributed to the ventilated segments of the lung, resulting in increased perfusion of the ventilated segments.

4.10.2 Many infants with parenchymal lung disease have elevated pulmonary arterial pressures. Premature therapy with early initiation of iNO prior to lung recruitment is not beneficial, and optimal lung inflation with adequate PEEP and/or surfactant often eliminates the need for iNO therapy.

4.10.3 Continuing iNO in infants unresponsive to iNO or failure to wean iNO can potentially lead to prolonged dependence on NO due to suppression of endogenous eNOS.

4.10.4 If left ventricular dysfunction is associated with high left atrial pressures and a left-right shunt at the level of the foramen ovale, in the presence of a right-to-left shunt at the ductus arteriosus, iNO is contraindicated because it may precipitate pulmonary edema and respiratory deterioration. An indicator (i.e. has both positive inotropic and vasodilator effects) such as milrinone should be initiated.

4.11 **Management of INO resistant PPHN** :

4.11.1 If iNO is not effective or not available and if hypoxemia persists:

4.11.1.1 Reassess ventilation to ensure adequate lung recruitment (with surfactant and/or optimal PEEP/MAP preferably with high frequency ventilator)

4.11.1.2 Consult cardiologist and repeat echocardiogram to evaluate ventricular function,cardiac output and severity of PPHN (and to rule out cyanotic CHD such as (TAPVR) that may have been missed on the first echocardiogram

4.11.1.3 Reassess hemodynamic status.

4.11.2 If blood pressure is relatively stable with good cardiac function:

4.11.2.1 Sildenafil(PDE 5 inhibitor):

4.11.2.2 Aerosolized Prostaglandin

4.11.2.3 Dobutamine

4.11.2.4 Like dobutamine, milrinone can be combined with iNO to augment pulmonary vasodilation while minimizing hypotension and tachyarrhythmia

4.12 **In the presence of systemic hypotension and good cardiac function**:

4.12.1 increase preload; Give saline 10-20 ml/kg up to two boluses

4.12.2 Dopamine if tissue perfusion does not improve, blood pressure is still low

4.12.3 Add norepinephrine if necessary

4.12.4 if still hypotension, add Hydrocortisone

4.12.5 Vasopressin (AVP): Endogenous vasopressin stimulates V1 receptors that mediate vascular tone (vasoconstriction), platelet function, and release of aldosterone and cortisol andV2 (vasodilatation) receptors that influence fluid balance and vascular tone. The potent vaso-constrictive effects of vasopressin dominate the cardiovascular response when it is used as an infusion.

4.12.6 Epinephrine: At low doses (0.01-0.1 mcg/kg/min) it stimulates the cardiac and vascular β1 and β2-receptors leading to increased inotropy, chronotropy, and peripheral vasodilation (primarily in the muscles).

4.13 Consider excessive mean airway pressure as a cause of hypotension and adjust it if possible

5. MATERIAL AND EQUIPMENT:

N/A

6. RESPONSIBILITIES:

6.1 Physician

6.2 Nurse

6.3 Cardiologist (who will do the Echocardiogram)

7. APPENDICES:

N/A

8. REFERENCES:

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9. APPROVALS:

	Name	Title	Signature	Date
Prepared by:	Ms. Afrah Saud Al Shammari	NICU Head Nurse		January 05, 2025
Prepared by:	Dr. Falah Nabhan Al Shammari	NICU Quality Coordinator		January 05, 2025
Reviewed by:	Mr. Sabah Turayhib Al - Harbi	Director of Nursing		January 07, 2025
Reviewed by:	Dr. Sarhan Hamdan Al Shammari	NICU Head of the Department		January 08, 2025
Reviewed by:	Mr. Abdulellah Ayed Al Mutairi	QM&PS Director		January 09, 2025
Reviewed by:	Dr. Tamer Mohamed Naguib	Medical Director		January 12, 2025
Approved by:	Mr. Fahad Hazam Al - Shammari	Hospital Director		January 19, 2025