GUIDELINE

Nitric Oxide Therapy (iNO)

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, 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 <u>disclaimer</u>

Also refer to Persistent Hypertension of the Newborn (PPHN)

Aim

To guide medical and nursing teams in timely diagnosis and management of conditions where iNO therapy is indicated.

Risk

Delayed commencement of iNO where indicated can lead to a delay in establishing adequate ventilation and many compromise cardiorespiratory function.

Indications

- Hypoxic respiratory failure despite "maximal medical therapy" i.e. Surfactant, sedation, conventional or HFOV/ HFJV with lung recruitment optimised, and therapy directed to maintenance of mean arterial blood pressure within the normal range commenced. An Oxygenation Index of more than 20 in term infants may also indicate a trial of iNO should be considered.
- Presence of persistent pulmonary hypertension of the newborn (PPHN). Ideally
 a cardiac echo should be performed before starting iNO, if this is not possible
 then one should be arranged after iNO commences.
- A cranial ultrasound should be performed if possible prior to commencing iNO therapy. A recent CXR may aid in assessing lung recruitment is optimised.

Key Points

- There is little trial evidence to support iNO use in preterm infants <34 weeks.
 <p>Although the subgroup of infants <34 weeks with prolonged rupture of membranes and pulmonary hypoplasia have been reported to show improvement with iNO therapy. iNO is used internationally in these infants as a "rescue" therapy in infants failing to improve oxygenation despite maximal medical therapy.</p>
- Care should be taken in infants with severe IVH or hypoxic ischemic encephalopathy, or in infants with coagulopathy.
- Prior to starting, discuss the use of iNO with parents prior to starting wherever possible.

Starting Dosage of iNO

Start <u>all</u> neonates with **20 parts per million (ppm).** After iNO use of 30-60 minutes medical staff to assess for response.

Positive response:

- Increase in PaO2 of ≥ 20mmHg.
- Or increase in Sp02 by 10%.
- Or able to drop Fi02 by 0.2.

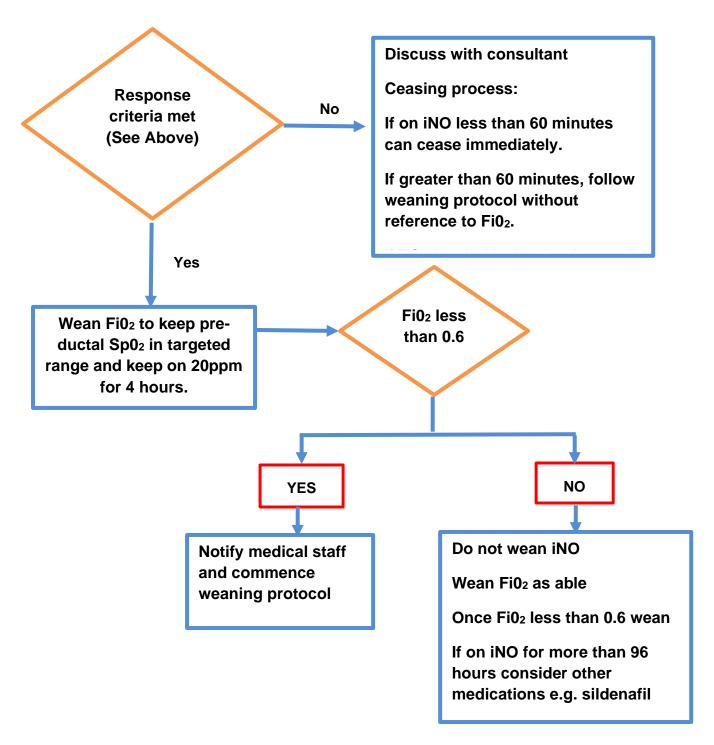
Partial response:

- Increase in PaO2 of 15-20 mmHg.
- Or Increase in Sp02 by 5-10%.
- Or able to drop Fi02 by at least 0.1-0.2.

If the neonate does not meet partial or positive response criteria discuss with consultant and in general iNO should be ceased. If the iNO has been started for less than 60 minutes, can cease immediately. The Consultant however has the discretion to continue.

If the iNO has been in situ for over an hour, follow weaning protocol without reference to Fi02. If the FiO2 rises during weaning call for medical review.

Ongoing iNO



Monitoring Met Hb

- Met Hb less than 2.5% is safe.
- MetHb 5-10% decrease iNO by 50%.
- MetHb more than 10% cease iNO.

Met Hb cannot bind with oxygen and transport it to the tissues. This results in the increased affinity of the unaffected haemoglobin for oxygen causing a left shift in the oxygen-dissociation curve leading to tissue hypoxia. Half-life of Met Hb is 55 min.

Met Hb has been shown to directly inhibit surfactant activity. Pulse-oximetry progressively overestimates oxygen saturation with increasing Met Hb concentrations and will not warn the clinician that a dangerous hypoxic state is developing.

Severe methemoglobinemia is treated with Methylene Blue.

Weaning

- After 4 hours of iNO assess for weaning. If Fi02 is less than 0.6 can start
 weaning. In certain other circumstances a consultant may choose to wean even
 if Fi02 is more than 0.6 is stability in Fi02 is achieved.
- In most circumstances iNO will be weaned first and then MAP. Discuss MAP weaning strategy with consultant.
- The weaning process involves a step wise process with repeated assessments for weaning failure.

Weaning failure is defined as:

- Increase in Fi02 by more than 0.2.
- Or Fall in Sp02 by more than 5%.
- Or pre/post ductal Sp02 gradient of more than 10% returns.
- If weaning failure occurs return iNO to previous dose then wait 4 hours before re-attempting to wean.
- Each weaning step should be considered 1-2 hours after the prior step if weaning criteria are met. If weaning a step is not successful, notify medical staff.

The step wise weaning process is:

- Decision by medical staff to commence weaning. Medical staff to document in the notes to wean as per protocol. Nursing staff can then follow protocol to wean each step without medical review. Nurses to notify medical staff if weaning failure occurs. See <u>Appendix 1: iNO Stepwise Weaning Process</u>
- 20ppm decreased to 10ppm.
- Assess for weaning failure.
- If none then after 2 hours reduce to 5ppm.
- Assess for weaning failure.
- If none then after 1-2 hours reduce to 4ppm.
- Thereafter reduce every 1-2 hours by 1ppm if no evidence of weaning failure at each step, until iNO ceased. Turn tank off.
- Consider increasing Fi02 by 0.1-0.2, 10 minutes prior to ceasing iNO.

Related CAHS internal policies, procedures, and guidelines

Persistent Pulmonary Hypertension of the Newborn (PPHN)
Methylene Blue.

Sildenafil.

References and related external legislation, policies, and guidelines

Barrington KJ, Finer N, Pennaforte T. Inhaled nitric oxide for respiratory failure in preterm infants. Cochrane database of systematic reviews (Online). 2017;1:CD000509.

Barrington KJ, Finer N, Pennaforte T, Altit G. Nitric oxide for respiratory failure in infants born at or near term. Cochrane database of systematic reviews (Online). 2017;1:CD000399.

Elmekkawi A, More K, Shea J, Sperling C, Da Silva Z, Finelli M, et al. Impact of Stewardship on Inhaled Nitric Oxide Utilization in a Neonatal ICU. Hospital pediatrics. 2016;6(10):607-15.

Soraisham AS, Harabor A, Shivananda S, Alvaro R, Ye XY, Lee SK, et al. Trends and Variations in the Use of Inhaled Nitric Oxide in Preterm Infants in Canadian Neonatal Intensive Care Units. Am J Perinatol. 2016;33(7):715-22.

Mullay R, McCallion N, El-Khuffash A. Inhaled nitric oxide in preterm neonates with preterm prelabour rupture of membanes, a systematic review. Acta Paediatr. 2023;112(3):358-71.

Ellsworth MA, Harris MN, Carey WA, Spitzer AR, Clark RH. Off-label use of inhaled nitric oxide after release of NIH consensus statement. Pediatrics. 2015;135(4):643-8.

Qureshi MA, Shah NJ, Hemmen CW, eta I. Exposure of intensive care unit nurses to nitric oxide and nitrogen dioxide during therapeutic use of inhaled nitric oxide in adults with acute respiratory distress syndrome. Am J Crit Care. 2003;12(2):147-53

Watcha MF, Connor MT, Hing AV. Pulse oximetry in methemoglobinemia. Am J Dis Child. 1989;143(7):845-47

Sahu KK, Dhibar DP, Gautam A, Kumar Y, Varma SC. Role of ascorbic acid in the treatment of methemoglobinemia. Turk J Emerg Med. 2016;16(3):119-120.

Sachdeva R, Pugeda JG, Casale LR, et al. Benzoncaine induced methemoglobinemia: a potentially fatal complication of transoesophageal echocardiography. Texas Heart Institute Journal. 2003;30(4):308-310.

Clinical Practice Guideline: Diagnosis and management of the infant with suspected or known pulmonary hypertension of the newborn. Brigham and Women's Hospital accessed on 11th October 2023

Jain A, Giesinger RE, Dakshinamurti S, et al. Care of the critically ill neonate with hypoxemic respiratory failure and acute pulmonary hypertension: framework for practice based on consensus opinion of neonatal hemodynamic working group. J Perinatiol. 2022;42:3-13

This document can be made available in alternative formats on request.

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Compassion

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Neonatology | Community Health | Mental Health | Perth Children's Hospital

20ppm After 4 hours of iNO 4 **Tolerated?** No Return to 10ppm Yes 20ppm 1 - 2 hours No Return Tolerated? to 10ppm 5ppm Yes 1 - 2 hours No Return **Tolerated?** to 5ppm Yes 4ppm 1 - 2 hours No Return **Tolerated?** to 4ppm 3ppm Yes 1 - 2 hours No Return **Tolerated?** to 3ppm 2ppm Yes 1 - 2 hours No Return Tolerated? to 2ppm 1ppm 1 - 2 hours

Appendix 1: iNO Stepwise Weaning Process

Failure to wean:

Stop weaning and return to previous dose if:

- Increase in Fi02 by 0.2
- Fall in Sp02 by more than 5%
- Increase in pre/post ductal Sp02 gradient of more than 10% returns

Yes

Wait more than 4 hours before reattempting to wean. If on iNO for more than 96 hours consider adding in medications such as <u>Sildenafil</u>.

Discontinue iNO