Inhaled Nitric Oxide Weaning

Neonatal Intensive Care Unit

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Center for Clinical Excellence

Inclusion Criteria:

- NICU infants ≥ 34 0/7 weeks GA at birth being treated with inhaled Nitric Oxide for PPHN
- Refer to PPHN guidelines for optimization of Respiratory Management

Exclusion Criteria:

- BPD
- CDH
- Pulmonary HTN team is consulted

FiO^2 weaning parameters:
Wean FiO^2 ~2-5% q 30 minutes for preductal sats >95% (or PaO^2>60mmHg)

SaO^2 ordered range:
92-97%

Weaning Failure Criteria:

Stop wean and return to the previous dose if any of the following occur:

- Preductal PaO^2 <50 or FiO^2 increases by >10
  OR
- Pre/Post ductal saturation gradient >10

iNO started at 20 ppm

After 60 minutes
Did preductal PaO^2 increase by ≥ 10mmHg ***or*** SaO^2 increase by ≥ 10?

No →
- Cardiopulmonary optimization
- Continue iNO at 20 ppm for **12** hours

Did preductal PaO^2 increase by ≥ 10mmHg ***or*** SaO^2 increase by ≥ 10?

Yes →
- Monitor ABGs.
- Wean FiO^2 as tolerated
- Continue iNO at 20ppm for **24** hours

No →
Unresponsive to iNO
Wean iNO every 15 minutes by 5ppm from 20ppm to 5ppm. Then by 1ppm until off.
End Pathway

Is FiO2 <50% ***and*** SaO^2 in ordered range?

No →
Notify Practitioner
- Continue iNO at current ppm until FiO^2 < 50%
- Escalate cardiopulmonary optimization per Acute PPHN* guidelines

Exit pathway if additional vasodilator added

Yes →
Wean iNO by 5ppm every 4 hours

Is FiO^2 <50% ***and*** SaO^2 in ordered range?

No →
Notify Practitioner
- Continue iNO at current ppm until FiO^2 < 50%
- Escalate cardiopulmonary optimization per Acute PPHN* guidelines

Exit pathway if additional vasodilator added

Yes →
Is iNO at 5ppm?

No →
Wean iNO by 5ppm every 4 hours

Yes →
Wean iNO by 1ppm every 4 hours
- If clinically feasible, do not wean FiO^2 while weaning iNO from 5ppm to off

Is FiO^2 <50% ***and*** SaO^2 in ordered range?

No →
- Increase to previous dose of iNO (*Some may require sequential increase if no response*)
- Once stabilized, maintain for at least 12 hours
- Optimize vent settings
- Consider ECHO and Pulm HTN team consult

Exit pathway if additional vasodilator added

Yes →
Is baby weaned off iNO?

No →
Wean iNO by 1ppm every 4 hours
- If clinically feasible, do not wean FiO^2 while weaning iNO from 5ppm to off

Yes →
End Pathway
Continue care as indicated

Inclusion & Exclusion Criteria

Inclusion Criteria

- NICU infants ≥ 34 0/7 weeks at birth being treated with inhaled Nitric Oxide for PPHN

Exclusion Criteria

- BPD
- CDH
- Premature infants < 34 weeks
- If Pulmonary HTN team is consulted

iNO Algorithm

Assessment & Monitoring

- Frequent Monitoring of Blood gases, preferably arterial
- Frequent calculation of OI with every blood gas
- Weaning FiO2 per parameters
- Ensure Cardiopulmonary optimization
- It is suggested that the lowest effective doses of iNO and O2 be used, to avoid excessive exposure to NO, Nitric dioxide (NO2), and methemoglobin (MetHb).
  - Check metHgb q 24 hours. If a patient is on iNO for 2 weeks, then the labs are spaced out to q.o.d
  - If metHgb > 5%, wean iNO if possible; if metHgb > 10%, treat with methylene blue, ascorbic acid after discussion with pharmacy.
- Nitric dioxide (NO2) alarm set NO2 alarm at 1 ppm.

iNO Algorithm

Treatments Not Recommended

- Doses greater than 20 ppm are not recommended
- Continuation of the pathway if additional vasodilator added
- Continuation of the pathway if no response as per the algorithm

iNO Algorithm

Risk Awareness & Zero Hero

Harmful impact on continuing iNO in the patient cohort that does not respond to iNO

iNO Algorithm

Key References

- Finer N, Barrington KJ. Nitric oxide for respiratory failure in infants born at or near term. *Cochrane Database of Systematic Reviews*. Published online October 18, 2006. doi:10.1002/14651858.cd000399.pub2
- Clark RH, Kueser TJ, Walker MW, et al. Low-dose nitric oxide therapy for persistent pulmonary hypertension of the newborn. *New England Journal of Medicine*. 2000;342(7):469-474. doi:10.1056/nejm200002173420704
- Spinale JM, Laskin BL, Sondheimer N, Swartz SJ, Goldstein SL. High-dose continuous renal replacement therapy for neonatal hyperammonemia. *Pediatric Nephrology*. 2013;28(6):983-986. doi:10.1007/s00467-013-2441-8
- Stenger MR. Hospital variation in nitric oxide use for premature infants. *Pediatrics*. 2012;129(4). doi:10.1542/peds.2011-1809d
- Davidson D, Barefield ES, Kattwinkel J, et al. Safety of withdrawing inhaled nitric oxide therapy in persistent pulmonary hypertension of the newborn. *Pediatrics*. 1999;104(2):231-236. doi:10.1542/peds.104.2.231
- Fischer H, Singh T, Devlin L, et al. A quality improvement project improving the value of Ino utilization in preterm and term infants. *Journal of Perinatology*. 2020;41(1):164-172. doi:10.1038/s41372-020-0768-0
- Nelin LD, Potenziano JL. Inhaled nitric oxide for neonates with persistent pulmonary hypertension of the newborn in the CINRGI study: Time to treatment response. *BMC Pediatrics*. 2019;19(1). doi:10.1186/s12887-018-1368-4
- DiBlasi RM, Myers TR, Hess DR. Evidence-based clinical practice guideline: inhaled nitric oxide for neonates with acute hypoxic respiratory failure. *Respir Care*. 2010 Dec;55(12):1717-45. PMID: 21122181.
- Finer NN, Sun JW, Rich W, Knodel E, Barrington KJ. Randomized, prospective study of low-dose versus high-dose inhaled nitric oxide in the neonate with hypoxic respiratory failure. *Pediatrics*. 2001;108(4):949-955. doi:10.1542/peds.108.4.949
- Thomas CA, Valentine K. Utility of routine methemoglobin laboratory assays in critically ill pediatric subjects receiving inhaled nitric oxide. *Journal of Critical Care*. 2018;48:63-65. doi:10.1016/j.jcrc.2018.08.014

iNO Algorithm

Quality Measures & Clinical Support Tools

Goals

1. Wean iNO appropriately and in a timely manner
2. Limit excessive use of iNO
3. Discontinue iNO when no response

Potential Areas of Research

Incidence of late responders and non-responders

Quality Measures

Outcome Measure

iNO utilization in number of hours

Process Measures

Process Measure 1: Utilization of the order set amongst those eligible (Was the order set used Yes No)

Process Measure 2: For patients where FiO^2 remains < 50% for 30 hours,

1. Was the iNO wean started (defined as any decrease in iNO)?
2. Was iNO discontinued during that timeframe of 30 hours?

Balancing Measure

1. Number of patients where iNO was restarted within 24 hours of discontinuation.
2. Rate of Methemoglobin level >10% in any patient on iNO

iNO Algorithm

Pathway Team & Process

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Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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iNO Algorithm