Inhaled Nitric Oxide (iNO) Weaning in the CICU

**ALGORITHM**

**Inclusion Criteria:**
Suspected or confirmed pulmonary hypertension and or right ventricular dysfunction requiring iNO for medical, postoperative or post-interventional reasons. Ventilated or extubated.

**Exclusion Criteria:**
Patients outside the CICU

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**Primary Interventions**
- Return to last stable iNO rate
- Increase FiO2 by 20%
- Check ABG or VBG, lactate and SvO2
- R/O residual lesions –
  - Echocardiography
  - If indwelling Swan-Ganz catheter: Qp/Qs estimation, CO, CI, SVR and PVR as required
- Re-assess inotropic drugs
- Evaluate for PAH Triggers
- Consider starting sildenafil PO. If oral intolerance, start sildenafil IV after the above have been addressed. See Sildenafil on back for dosing instructions.

**Secondary Interventions**
- Return to last stable iNO rate
- Start Sildenafil PO. For oral intolerance start IV infusion. See Sildenafil on back for dosing instructions.
- Reassess Readiness Criteria until tolerance of 2nd PO dose or 4 hours after the inception of the infusion

**Tertiary Interventions**
- Return to last stable iNO rate
- Remain on Sildenafil
- Consult Cardiology PAH team for complementary evaluation and therapy

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**Phase 1 Weaning**
40ppm – 10ppm
- Decrease by 10ppm every 30-60 min
- *For severe PAH consider 30-120min
- Tolerated
- Not Tolerated

**Phase 2 Weaning**
10ppm-5ppm
- Decrease by 5ppm every 30-60 min
- *For severe PAH consider 30-120min
- Tolerated
- Not Tolerated

**Phase 3 Weaning**
Below 5ppm
- Decrease by 1ppm every 30 min
- *At 2ppm, increase FiO2 by 20% to a max of 60%
- *For severe PAH consider 30-120min
- Tolerated
- Not Tolerated

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**Weaning Instructions**
- After the ‘Primary Interventions’ have already been completed, then go directly to ‘Secondary Interventions’.
- If ‘Secondary Interventions’ have already been completed, then go directly to ‘Tertiary Interventions’.
- Stop iNO and observe for 4 hours
- Restart iNO at 5ppm
- Wean FiO2

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**Off Pathway:**
Weaning instructions per Cardiology PAH team
Extubation Criteria:
If ventilated, iNO less than or equal to 20ppm and adequate readiness criteria
- Consider extubation and
- Administer latest iNO rate X2 via nasal prongs upon extubation
- Wean iNO per algorithm at Phase 1

Readiness Criteria for Starting iNO Wean:
Key Factors –
- FiO2 less than or equal to 60%
- Hemodynamically stable for greater than or equal to 6 hours
- No PAH triggers
Ancillary Factors –
- MPAP less than or equal to 50% MAP
- Normal Lactate
- DavO2 less than or equal to 30

Weaning Tolerance Criteria:
- 20% or less decrease in PaO2 -OR- 10% or less decrease in sPO2 AND FiO2 less than or equal to 60%
- No PAH rebound (MPAP less than or equal to 50% MAP)

PAH Triggers (selected):
- Volume overload/pulmonary edema
- Anemia
- Pain/agitation
- Acidosis

Sildenafil:
Start sildenafil PO with a goal of 1mg/kg/dose q6-8 hours:
- 1st dose of 0.5mg/kg (max dose 10mg)
- 2nd dose of 0.75mg/kg (max dose 15mg)
- 3rd dose of 1mg/kg (max dose 20mg)
For oral intolerance start sildenafil IV:
- Less than or equal to 15kg:
  - 0.07 mg/kg/hr
- More than 15kg - Intermittent IV infusion with a goal of 0.5 mg/kg/dose every 8 hours:
  - 1st dose of 0.25 mg/kg (max does 5mg)
  - 2nd dose of 0.38 mg/kg (max dose 7.5mg)
  - 3rd dose of 0.5 mg/kg (max dose 10mg)
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TARGET POPULATION

Inclusion Criteria
Suspected or confirmed pulmonary hypertension and or right ventricular dysfunction requiring iNO for medical, postoperative or post-interventional reason. Ventilated or extubated.

Exclusion Criteria
Patients outside the CICU

BACKGROUND | DEFINITIONS

Background:

- Medical, postoperative or post-interventional cardiac patients in need of iNO require cautious and yet assertive weaning of the latter in order to preserve hemodynamic stability and avoid potentially life-threatening rebound pulmonary hypertension
- There is a need for consistent and objective practices for the iNO weaning process
- Use iNO with caution in patients with suspected Pulmonary Venous Obstructive Disease (PVOD) or left ventricular dysfunction as it may increase pulmonary capillary blood volume leading to pulmonary edema and/or enhance the severity of the patient’s heart failure
- Use of iNO in patients with Right-to-Left dependent blood flow may be contraindicated
- Goal is to safely wean the iNO as soon as deemed possible and safe
- Consider that abrupt discontinuation of iNO may cause rebound pulmonary hypertension
- Before weaning, patients must:
  - Fulfill “Readiness Criteria”
  - Be free of “Pulmonary Arterial Hypertension (PAH) triggers”
- Extubation is to be considered if the patient fulfills the “Extubation Criteria”
- Weaning guidelines are based on a three phase algorithm
Definitions:
- iNO - Inhaled Nitric Oxide
- FiO2- Inspired oxygen fraction
- DaVO2- Arterial-venous oxygen difference/oxygen debt
- PaO2 – Partial pressure of oxygen
- sPO2- Peripheral capillary oxygen saturation
- SvO2- Mixed venous oxygen saturation
- PAP - Pulmonary Artery Pressure
- PAH- Pulmonary Arterial Hypertension
- PwP- Pulmonary Wedge Pressure
- PVR- Pulmonary Vascular Resistance
- MAP- Mean Arterial (systemic) Pressure
- MPAP – Mean Pulmonary Artery Pressure

Extubation Criteria:
If iNO less than or equal to 20ppm and adequate readiness criteria:

- Consider extubation and
- Administer latest iNO rate X2 via nasal prongs upon extubation
- Wean iNO per algorithm at Phase 1

Readiness Criteria for Starting iNO Wean:
- Key Factors
  - FiO2 less than or equal to 60%
  - Hemodynamically stable for greater than or equal to 6 hours
- Ancillary Factors
  - MPAP less than or equal to 50% MAP
  - No lactic acidosis
  - DaVO2 less than or equal to 30

Weaning Tolerance Criteria:
- 20% or less decrease in PaO2 –OR – 10% or less decrease in sPO2 –AND- FiO2 less than or equal to 60%
- No PAH rebound (MPAP less than or equal to 50% MAP)

PAH Triggers (selected):
- Volume overload/pulmonary edema
- Anemia
- Pain/agitation
- Acidosis
INITIAL EVALUATION

- Oxygen Saturation
- MPAP, PwP
- Vital Signs - Systemic BP, HR, RR
- Color
- Perfusion
- Near Infra-Red Spectroscopy (NIRS)
- SvO2 and DaVO2

LABORATORY STUDIES | IMAGING

- Echocardiography to assess for signs of PAH, ventricular function, cardiac repair and to rule-out residual lesions
- ABG to access pH, ventilation and oxygenation
- Lactate and SvO2 to evaluate tissue perfusion and DaVO2
- CXR to access lung expansion and to rule out intra-thoracic “PAH triggers”
- Bed-side hemodynamic evaluation via the Swan-Ganz catheter (Qp/Qs, MPAP, PwP, CO, CI, PVR, SVR), the trans-thoracic pulmonary catheter and/or the left atrial catheter when indwelling

Note: patients with persistent iNO-dependent PAH and/or hemodynamic instability and/or suspicion of residual lesions, may require a cardiac catheterization prior to weaning the iNO

BEFORE WEANING THE INO:

- In patients with prior medical therapy for PAH, home medications should be resumed before weaning, as long as tolerated by enteral or parenteral administration
- Maintain adequate ventilation, oxygenation, and pH; Hypoxia, Hypercarbia, and acidosis may increase PVR and worsen PAH
- Avoid agitation and stressful procedures during weaning of iNO
- Consider extubation if fulfilling “Extubation Criteria”; if applicable, double the latest amount of iNO (in ppm) via nasal prongs
- Maintain stable hemodynamics
- Assess iNO Weaning “Readiness criteria”

DURING THE INO WEANING:

- Evaluate “Weaning Tolerance Criteria”
- **Phase 1** weaning includes completion of the primary interventions with the first round of non-tolerance of sequential reduction of iNO:
  - Return to last stable iNO rate
  - Increase FiO2 by 20% to a maximum of 60%
  - Check ABG or VBG, lactate and svO2
  - Rule out residual lesions
    - Echocardiography
    - If indwelling Swan-Ganz catheter: Qp/Qs estimation, CO, CI, SVR and PVR as required
- Re-assess inotropic drugs
- Evaluate for “PAH Triggers”
- Consider starting Sildenafil PO or IV after the above have been addressed
  - Wait 4 hours, then reassess “Readiness Criteria” and begin again at Phase 1 weaning if ready

- **Phase 2** weaning includes the consideration of all primary interventions and starting sildenafil with the second round of non-tolerance of sequential reduction of iNO according to the following schedule:
  - Start PO sildenafil with a goal of 1mg/kg/dose every 6-8 hours (see algorithm above)
  - For PO intolerance, start IV sildenafil (see algorithm above)
  - Wait for tolerance of the second dose or at 4 hours after the inception of the IV infusion reconsider the “Readiness Criteria” and begin again at Phase 1 weaning if ready

- **Phase 3** weaning includes consideration of the primary interventions, continued Sildenafil, and consultation of the Cardiology PAH team with the third round of non-tolerance of sequential reduction of iNO

**AFTER THE INO WEANING:**

- Continue to assess weaning tolerance criteria for 4 hours
- If stable, start weaning FiO2
REFERENCES

5. Walsh BK, Rettig JS. Implementation of an inhaled nitric oxide protocol: a paradox or the perfect pair? Respir Care. 2015;60(5):760-1.
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Clinical Care Guideline and Measures Review Committee – September 13, 2016
Medication Safety Committee – Not applicable
Antimicrobial Stewardship Committee – Not applicable
Pharmacy & Therapeutics Committee – August 25, 2016

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REVIEW | REVISION SCHEDULE

Scheduled for full review on September 13, 2020
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