Operating Instructions for Inhaled Nitric Oxide Therapy

Purpose

To provide guidelines for the initiation of inhaled nitric oxide therapy via the NOxBOX delivery system by completing the pre-use system purge and performance test.

Audience

Physicians, Nursing staff, and Licensed Respiratory Care Practitioners.

Scope

Inhaled Nitric Oxide is a selective pulmonary vasodilator. Nitric Oxide, the active substance in NOxBOX is a gaseous blend of 0.08% NO and 99.2% Nitrogen respectively for 800 ppm concentration.

Physician's Order

Physician orders must include the following:

- Mechanical ventilation parameters
- Nitric Oxide concentration in ppm
- Methemoglobin levels are recommended at 1 hour and 8 hours after initiation of therapy and at physician discretion.

Indications

Inhaled nitric oxide therapy is indicated in term and near-term (>34 weeks) neonates with hypoxic respiratory failure that is associated with:

- Meconium aspiration syndrome (MAS)
- Pneumonia/ Sepsis
- Persistent Pulmonary Hypertension of the Newborn (PPHN)
- Congenital Diaphragmatic Hernia (CDH)
- Respiratory Distress Syndrome (RDS)
- Off label use for post-op Cardiac Patients such as LVAD
- Respiratory Failure (ARDS)

Adverse Effects

Goals The goals of delivering inhaled nitric oxide are to:

- Improve and maintain oxygenation
- Reduce the need for extracorporeal membrane oxygenation (ECMO)
- Relieve primary pulmonary artery hypertension

The adverse effects associated with inhaled nitric oxide therapy include:

Equipment

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- Rebound (abrupt discontinuation of INO may lead to worsening oxygenation and increasing pulmonary artery pressure)
- Methemoglobinemia (increases with dose of INO)
- Increased levels of NO_2
- Inhaled nitric oxide therapy should not be used in patients that are dependent on right-to-left shunting of blood

- NOxBOX delivery system
- NO cylinders with > then 200PSI

Procedure

Pre-Use System Purge and Performance Test

Step	Action
1	Turn On NOxBOX. Low calibration automatically starts following the NOxBOX self-test. Check the NOxBOX gas cylinders for the correct product identity labels, cylinder concentration, and expiration date. Ensure that at least one NOxBOX gas cylinder with more than 50 psig is available
2	Connect one of the high pressure regulators to an NOxBOX cylinder and tighten the fitting to the cylinder
3	Connect the regulator hose to one of the inlets
4	If using the NOxBOX blender with the system, connect the oxygen hose to the outlet.
5	Ensure water trap bottle and water separator cartridge are in place.
6	Connect all the proper connects. (NOxBOX injector, sample line, etc.)
7	Open and then close the cylinder valve.
8	Check for adequate cylinder pressure, if no pressure decrease is observed in 30 sec., high pressure leak test is complete.

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9	Confirm injector module is out of patient breathing circuit or pre use circuit. Press NEXT button to start the purge process. Low cylinder pressure alarm may activate. Open cylinder valve when purge is complete.
10	Backup iNOmax Delivery test: • Turn the back iNOmax delivery ON (250mL/min) • "Backup ON" alarm will occur • Allow 2-3 minutes for the monitored values to stabilize and make sure the NO and NO2 readings are within the following ranges: **NO = 14-26 ppm NO2 = <1.0 ppm** • Turn the backup iNOmax delivery OFF
11	Performance Test Assemble the pre-use set up connectors and tubing (press show diagram button if needed). Set the Oxygen flowmeter to 10 L/min. Press NEXT button to automatically set the INOMAX dose to 40ppm. Allow values to stabilize Compare the iNOmax DSIR monitor values to the values below: **NO = 35-45 ppm NO2= <1.5 ppm FiO2 = ≥92** **Performance Test is complete**. The iNOmax is automatically set to zero.
12	iNOblender Test: • Remove the Pre-Use set-up oxygen tubing from the oxygen flowmeter and connect it to the front of the iNOblender. • Remove the Injector Module from the Pre-Use set-up and reconnect the adapters. • On the iNOblender, set the iNOmax dose to 40 ppm and the O2 flow to 10L/min. • Verify that the monitored value for NO is within the following range: **NO= 32-48 ppm** • Turn the dose and flow to zero and remove the Pre-Use set-up from the iNOblender

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13	Purge the Regulator Supply Line: • If not immediately connecting to a patient, turn the iNOmax cylinder OFF. • Purge the pressure from the regulator using the purge port on the back of the iNOmax DS unit. • Reconnect the regulator line to the iNOmax DS inlet. • If the iNOmax DS unit is depressurized and not used within 12 hours, repeat the pre-use procedure.

Initiation of Therapy with Conventional Mechanical Ventilation, Infant Nasal CPAP (NCPAP), and High Flow Nasal Cannula Systems (HFNC)

Step	Action
1	Perform pre-use system purge and performance test as outlined above
2	Insert the Injector Module on the dry side of the breathing circuit prior to the humidifier (following the directional arrow located on the Injector Module) using a 15mm and 22mm adapter.
3	**Neonatal Application** Insert 6” extension tubing with sample tee adapter at the patient wye on the inspiratory side of the breathing circuit distal to the temperature probe adapter. This extension tubing minimizes sampling of mixed inspiratory/ expiratory gases (6” extension tubing **NOT NEEDED** for NCPAP or HFNC) **Adult Application:** Insert a Sample Tee Adapter on the inspiratory side of the breathing circuit, and connect the sample tee adapter to the gas sample line.
4	Set the iNOmax dose to be delivered to the patient.

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5	After the monitored values have stabilized, set or change the user-adjustable alarms to the appropriate ranges. **NO_2 high alarm should be set at 3.0 ppm** **NO alarms should be set ± 5 ppm of desired level**
6	Attach an appropriate sized resuscitation bag to the iNOblender for the manual delivery of NO.

Initiation of Therapy with High Frequency Oscillatory Ventilation (HFOV)

Step	Action
1	Perform pre-use system purge and performance test as outlined above
2	Assemble Injector Module for patient delivery of NO as outlined in the Delivery System pocket guide (page 37-38). Ensure the injector module is on the dry side of the heater. **Note: Omission of the one-way valve may result in high NO delivery.**
4	Insert patient gas sample line connection as outlined in the Operation Manual using a 90° luer elbow adapter.
5	After connecting the iNOmax delivery system to the patient HFOV Circuit, set the nitric oxide dose to be delivered.
6	After the monitored values have stabilized, set or change the user-adjustable alarms to the appropriate ranges. **NO_2 high alarm should be set at 3.0 ppm** **NO alarms should be set ± 5 ppm of desired level**
7	Attach an appropriate sized resuscitation bag to the iNOblender for the manual delivery of NO.

Assessment of Outcome

1. Arterial, venous and capillary blood gas values
2. Pulse oximetry
3. Pulmonary artery pressures

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Monitoring during iNO

The risk of methemoglobinemia increases with the dose of nitric oxide. In clinical trials, the maximum methemoglobin levels were typically reached 8 hours after the initiation of therapy, though peak levels were seen as late as 40 hours after the start of therapy (iNO package insert, 2014).

Methemoglobin Range	Action
>10%	Discontinue iNO, repeat metHb every 2 hours until <5%; if needed, restart therapy at 50% of the iNO at discontinuation
5-10%	Wean iNO by 50% and repeat metHb in 2 hours; repeat sequence until metHb is <5%
<5%	No Action Needed

Infection Follow procedures as outlined Healthcare Epidemiology Policies and **Control** Procedures: #2.24 Respiratory Care Services.
http://www.utmb.edu/policy/hcepidem/search/02-24.pdf

Use of Inhaled Nitric Oxide (iNO)

Clinical Practice Guideline

Definitions (Jumar 2007, Carriedo 2003)

Responder: A patient is classified as a responder to iNO therapy if the post-ductal PaO_2 increases 20mmHg within 30 minutes of starting iNO without any change in the inspired oxygen concentration. If there is no increase with the initial dose (5-15 ppm), iNO should be increased to 20 ppm.

Non-Responder: If, after 30 minutes at 20 ppm, the post-ductal PaO_2 does not increase >20mmHg, the patient is classified as a non-responder and therapy should be discontinued, as follows:

Recommended Weaning Strategy for Discontinuation of iNO – Non-Responders	
Time (min)	iNO Concentration (ppm)

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0	20
30	10
60	5
90	2
120	0

- The patient should be classified as a responder or a non-responder after <1 hour of iNO. Non-responders should start the weaning process, as above.
- An increase in O_2 saturation >10% will be considered equivalent to an increase in PaO_2 >20 mmHg.

Weaning from iNO (Davidson, 1999**)**

Responders may be weaned from iNO when any of the following conditions are met:

- PaO_2 >60 on FiO_2 <.60
- Oxygenation Index (OI) <10

- If PaO_2 or SpO2 falls >10% mmHg after any weaning step, the dose of iNO may be increased back to the previous dose, with appropriate increases in FiO_2

Recommended Weaning Strategy for Discontinuation from iNO therapy – Responders*				
Time (hours)	iNO Concentration (ppm)			
0 (Start of Wean)	5	10	15	20
1	4	5	10	15
2	3	4	5	10
3	2	3	4	5
4	1	2	3	4
5	0	1	2	3
6	-	0	1	2
7	-	-	0	1
8	-	-	-	0
Total	5	6	7	8

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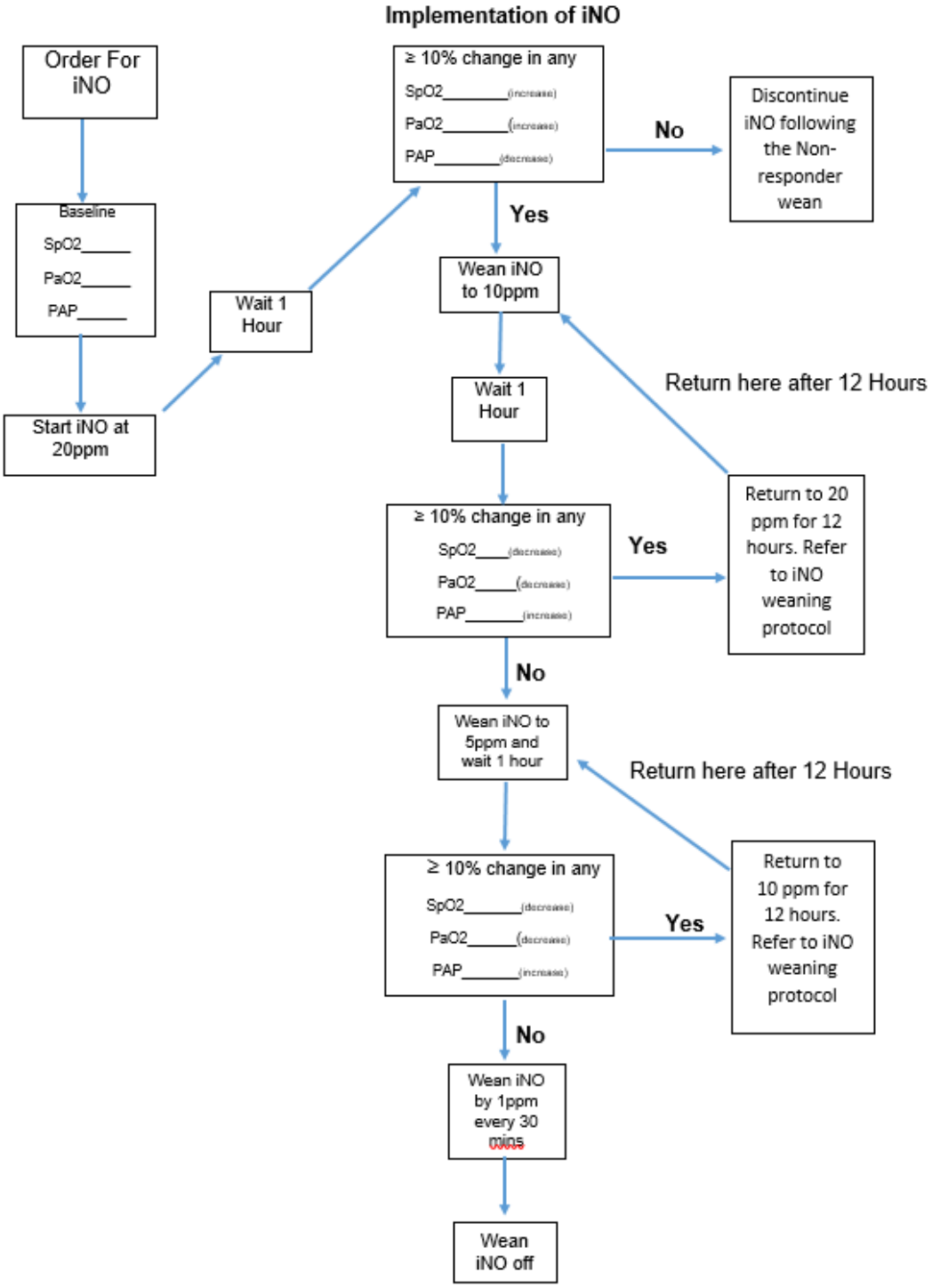

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**Deviations from this strategy may be indicated if the patient is particularly sensitive to changes.*

Safety Precautions

Oxygen safety techniques as outlined in the iNOmax Manual will be followed.

All alarms on ventilators will be activated at all times.

All alarms on INOvent delivery system will be activated at all times.

References

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