



Critical Care Therapy and Respiratory Care Section

Category:	Clinical
Section:	Medicinal Gas Therapy
Title:	INOPulse Delivery System
Policy #:	03
Revised:	07/01

1.0 PROCEDURE: Nitric oxide delivery via the Ohmeda INOpulse portable delivery system in ambulatory patients.

2.0 DEFINITION/DESCRIPTION:

Nitric oxide (NO), not to be confused with the anesthetic nitrous oxide, is a gas molecule with selective vasodilation properties. NO is the active metabolite of a number of vasodilators, including sodium nitroprusside and nitroglycerin. It is also produced in all human organ systems, including the nasopharynx and lungs.

In high concentrations, NO is profoundly toxic and caused diseases identical to Acute Respiratory Distress Syndrome (ARDS). In the presence of oxygen, NO is broken down to form nitrogen dioxide (NO₂). In the blood, NO interacts with hemoglobin. The by-product of this reaction produces increased levels of methemoglobin. Methemoglobin will not carry oxygen, and therefore, its level must be closely monitored during NO therapy.

Inhaled NO is a selective pulmonary vasodilator, which decreases pulmonary vascular resistance (PVR) and improves gas exchange. Current methods of administration of NO are complicated and not without hazard. NO is stored in concentrations of 100 to 10,000 ppm, with nitrogen gas. Safe and effective concentrations of inhaled NO range from 1 to 40 ppm, which are achieved by mixing NO with respiratory gases. The flow rate of the mixed gases is carefully matched to the rate of ventilation, preventing buildup of NO₂. While straightforward for ventilated patients, ambulatory patients who may vary their rate of ventilation render delivery difficult.

The INOpulse delivery system is an alternative method of delivering NO which injects a small volume of NO at the start of each breath. The small portable unit connects to a small gas cylinder that delivers NO via a nasal cannula allowing a patient to be ambulatory. It is an investigational device that is being implemented in various studies to determine the efficacy of its dosage capabilities in treating secondary pulmonary hypertension.

3.0 SETTINGS

Personnel trained and competent in this procedure will initiate nitric oxide therapy via the Ohmeda INOpulse Delivery System. In reference to policy # 02, entitled *Nitric Oxide Therapy*, section 3.1.1, the CCTRCS staff can administer NO in support of research protocols. The following protocols have been approved by the review board to administer NO using the INOPulse:

3.1 Inhaled Nitric Oxide Therapy for Patients with Sickle Cell Anemia and Secondary Pulmonary Hypertension (Protocol # 01-CC-0223).

3.1.1 Objective: 1) To determine the pathophysiological processes that is associated with and potentially contribute to secondary pulmonary hypertension in adult patients with sickle cell anemia. 2) To determine the relative acute vasodilatory effects of oxygen, intravenous prostacyclin, and inhaled nitric oxide on pulmonary artery pressure and other hemodynamic parameters in patients with secondary pulmonary hypertension and sickle cell anemia. 3) To determine the effects of two months of inhaled nitric oxide on pulmonary pressures, other hemodynamic parameters, exercise tolerance, and symptoms in this patient population.

3.2 Nitric Oxide Inhalation Therapy for Myocardial Ischemia in Patients with Coronary Artery Disease (Protocol # 01-H-0140).

3.2.1 Objective: 1) To demonstrate the effectiveness of NO inhalation therapy for the relief of inducible myocardial ischemia and effort angina in patients with coronary artery disease (CAD) who have failed attempts at conventional medical and revascularization (catheter-based or surgical therapy). 2) To provide mechanism for such an effect. The hypothesis is that NO inhalation therapy will improve the coronary blood flow response to stress, thus relieving myocardial ischemia, by dilating the coronary circulation deficient in local NO synthesis, by preventing platelet activation, and by reducing vascular inflammation.

4.0 INDICATIONS

- 4.1 To reduce pulmonary artery pressures due to pulmonary hypertension
- 4.2 To reduce pulmonary vascular resistance
- 4.3 To enhance oxygenation

5.0 CONTRAINDICATIONS

5.1 Absolute contraindication:

- 5.1.1 Patients with congenital or acquired methemoglobinemia reductase deficiency

5.2 Relative contraindications:

- 5.2.1 Patients with bleeding diathesis
- 5.2.2 Intracranial hemorrhage
- 5.2.3 Severe left ventricular failure

6.0 HAZARDS/COMPLICATIONS

- 6.1 Elevated methemoglobin levels
- 6.2 Nitrogen dioxide (NO₂) toxicity
- 6.3 Prolongation of PT/PTT
- 6.4 Increased left ventricular filling associated with rapid changes in pulmonary pressures
- 6.5 Rapid withdrawal of NO may result in rebound hypoxemia and pulmonary hypertension

7.0 PRECAUTIONS

- 7.1 Use of this device lowers FiO₂.
- 7.2 To minimize exposure to NO₂, do not put the cannula on the patient until step 3 of “To Start Nitric Oxide Delivery”
- 7.3 During INOPulse delivery system use, a separate INOpulse delivery system should be available as a backup
- 7.4 Always replace batteries in pairs, using alkaline “C” batteries only
- 7.5 Patients who mouth breathe may not trigger this device

8.0 USING THE SYSTEM

8.1 System Overview

- 8.1.1 Delivers small pulses of 100 ppm (or less) therapeutic NO to the patient via a nasal cannula
- 8.1.2 Functions by delivering a pulse volume dose of NO established by a clinician at the beginning of each patient inspiration, as triggered by sub-atmospheric pressure
- 8.1.3 Offers two INOPulse system variants, depending on the dose setting range required:
 - 8.1.3.1 High Dose Range (15 mL to 60 mL; in 5mL increments)

Note: We will only be using the high dose range portable unit.

8.1.3.2 Low Dose Range (3 mL to 10 mL; in 1 mL increments)

8.1.4 Includes added safety features:

8.1.4.1 Automatic purge function to minimize NO₂ production. When turned to on or to standby, the system is automatically purged of NO₂, which may have formed by NO flowing through the system.

8.1.4.2 A green LED breath-detection indicator lights up on the left when a breath is detected and the system is sending a pulse on NO. If the system does not detect a breath in 10 to 15 seconds, it automatically delivers a pulse of NO to minimize the formation of NO₂ (no green flashing LED).

8.1.4.3 A set of alarms (indicated on the right by a red flashing LED and audible tone) designed to monitor correct operation including:

“Open Cylinder”	“Low Batteries”
“Close Cylinder”	“Low Supply pressure”
“Breath Not Detected”	“System Failure”

8.1.4.4 A dose-setting procedure that helps prevent the patient from accidentally changing the set dose. Unmarked buttons provide access to the Setting Mode and a sequence of the alarm LEDs indicate the current dose setting.

8.1.5 Can also be used with supplemental nasal oxygen therapy using only Datex-Ohmeda dual nasal cannulas.

8.2 Pre-Use Check

8.2.1 Check that the hose and cannula are in good condition.

8.2.2 Check that a spare gas cylinder and batteries are available.

8.2.3 Check that the regulator inlet seal is present and shows no sign of wear.

8.2.4 Check that you have the correct dose range model (‘3-10 mL’ or ‘**15-60 mL**’ on the front label.) We will be using the 15-60ml unit.

8.2.5 Check for the correct dose setting by pressing and holding the SET button.

8.2.6 Check for the correct alarm setting by pressing and holding the ACCEPT button.

8.2.7 Connect the INOPulse delivery system. An optional extension hose can be used as shown on page 12 or 18 of the INOPulse delivery system Operation Manual

8.2.8 To use the system continue with the following steps of “To Start Nitric Oxide Delivery” which include additional steps of this Pre-Use Check.

8.3 To Start Nitric Oxide Delivery

Important: Do not open cylinder valve until ready to start NO delivery. For correct NO delivery, do not insert cannula into the nose until the system has been correctly turned on.

- 8.3.1 Open the cylinder valve and check that gas is not flowing from the device or cannula. *
- 8.3.2 Press the ON button and make sure that all LEDs turn on and a tone sounds. The red LED turns on as the system purges. **
- 8.3.3 After the green LED goes out and the tone stops, the device is ready for use. Put on the cannula so it is comfortable.
- 8.3.4 * **Important:** The cylinder-pressure gauge must be in the green operating zone when the cylinder valve is open.
- 8.3.5 ** **Purge time:** low range unit =25seconds/purges about 700cc; high range = 5 seconds/purges about 700cc.

8.4 To Stop Nitric Oxide Delivery

Important: Do these steps **Exactly** to Stop Nitric Oxide Delivery

- 8.4.1 Remove the cannula from the nose.
- 8.4.2 Press and hold the Standby button for at least one second until a tone sounds.
- 8.4.3 Within 10 seconds, close cylinder valve. The red LED turns on as the system purges.

9.0 STANDARD PROCEDURES

9.1 Changing dose level and “Breath not detected” alarm

- 9.1.1 Note: Adjustments can be made with the control unit in Standby or On.
- 9.1.2 Note: Use three fingers to complete the following two steps.
- 9.1.3 Press and hold the SET and the ACCEPT buttons for at least two seconds and continue holding these buttons through the next step.
- 9.1.4 When a tone sounds continue holding SET and ACCEPT buttons and press the STANDBY button within 3 seconds for at least 1 second. Release all three buttons when a tone sounds and the green LED flashes.
- 9.1.5 Press the SET button until dose level you want is indicated. See table on following page.

(picture of dose table)

- 9.1.6 Press the ACCEPT button to enter the dose setting and advance to the next function: the “Breath not detected” alarm selection.
- 9.1.7 Press the SET button to set the breath detection alarm.
- 9.1.8 Press the ACCEPT button to save the dose and alarm settings and exit the Setting mode.
- 9.1.9 If the control unit is on, you have 15 seconds to do steps 1-6. Otherwise, in Standby you have 60 seconds to do steps 1-6.
- 9.1.10 If the control unit is on at the start of the steps and times out (15 seconds) during the steps, the control unit automatically pulses the previous dose setting.
- 9.1.11 If you let the unit time out before completing all the steps, the unit keeps the previous dose and alarm settings. In either case, if the unit times out, do the steps again if you want to make changes.
- 9.1.12 NOTE: You can't enter the setting mode if an alarm condition is active.

9.2 Attaching gas cylinder

- 9.2.1 Make sure the control unit is in Standby.
- 9.2.2 Remove the regulator (if attached).
- 9.2.3 Check that the regulator inlet seal is present and shows no sign of wear.
- 9.2.4 Attach the regulator to cylinder.
- 9.2.5 Cylinder pressure gauge should be in the green normal operating zone.
- 9.2.6 Replace cylinder when pointer is in the red zone.

(picture of cylinder gauge)

9.3 Cylinders Sizes/Usage Formula

- 9.3.1 “88” size cylinder is 39 lbs empty, 44 lbs full and has a usable volume of = 1767L
- 9.3.2 “D” size cylinder is 8 lbs empty and full and has a usable volume of = 315 liters
- 9.3.3 Formula: Full cylinder/(RR x INOPulse setting) = minutes of use (divide by 60 for hours of use)

Example: Assuming RR 20BPM and NO dose at 40mL:
 $1767L / (20 \times 40ml) = 1767 / 0.8 \text{ LPM} = 2208 \text{ minutes or } 36+ \text{ hours}$

9.4 Connecting control unit inlet hose to regulator

- 9.4.1 Connect the control unit to the regulator assembly directly or with an extension hose.
- 9.4.2 Push the connector on until it “clicks.”
- 9.4.3 To disconnect, pull back on the knurled sleeve of connector. Do not pull on the soft cable portion.

9.5 Connecting the cannula

- 9.5.1 **Use only cannulas supplied by Datex-Ohmeda for this product to ensure material compatibility with nitric oxide delivery gas.**
- 9.5.2 Push the nasal cannula over the connector on the control unit.
- 9.5.3 Insert the nasal tips into the nostrils with the two plastic tubes over the ears and under the chin. Important: For correct NO delivery, do not insert the cannula into the nose until the system has been correctly turned on.
- 9.5.4 Adjust the plastic slide until the cannula is secure. The cannula nasal tips may be trimmed with scissors to fit. Important: Do not open the cylinder valve until ready to start NO delivery.
- 9.5.5 Important: The purging volume is enough for a single length of cannula tubing 5ft-7ft and the INOPulse extension hose. If additional length is required for mobility, the extension hose (connected between the gas cylinder and INOPulse unit) should be used. The extension hose is 35ft. **Utilization of extra lengths of oxygen supply tubing (between the INOPulse unit and the patient nose) is not recommended as sensing of the patient breath could be altered and the purging volume not enough to clear the extra length.**

9.6 Changing the batteries

- 9.6.1 Batteries can be changed while the control unit is on and powered by the external power supply without interrupting therapy. Otherwise, if the control unit is running on the batteries, place it in Standby to change the batteries.
- 9.6.2 Slide the battery door latch in the direction of the arrow to open the door.
- 9.6.3 Replace the batteries, always in pairs. Use only type “C” alkaline. Be sure to insert the batteries with the + and – ends as shown.
- 9.6.4 If the batteries are removed or left out and the external power supply is not in use, a single repeated tone might occur after one minute and be repeated for several minutes.
- 9.6.5 Battery life is affected by respiratory rate and dose setting. Generally the batteries will last about 72 hours of continuous use. The low battery indicator is initiated when there is approximately 2 hours left. It will continue to alarm until batteries are changed.
- 9.6.6 CCTRCS staff will be responsible for changing out the batteries every 48 hours on dayshift. A check off sheet needs to be initialed to ensure compliance of procedure.
- 9.6.7 **Important:** Batteries are not being charged when the external power supply is used.
- 9.6.8 **Important:** If the external power supply is disconnected or fails, the unit operates on batteries; always have batteries installed in the control unit.

9.6 Alarm information

- 9.7.1 Disconnect the INOPulse delivery system from the patient before troubleshooting.
- 9.7.2 Alarms are high priority requiring immediate attention. If you hear a series of beeps, check the front panel for a flashing red LED and follow the applicable recommended actions located on page 20 of the INOpulse Delivery System Operation Manual.
- 9.7.3 If unit is alarming “system failure”, discontinue the device and replace with backup unit which will be located by patient bedside. Notify research nurse.

9.7 Cleaning

Clean the exterior of the control unit and regulator with isopropyl-alcohol dampened cloth. **Do not allow liquid to enter any system components.**

10.0 DOCUMENTATION

- 10.1 Obtain order to perform all of the above procedures.
- 10.2 Chart results under Respiratory Consult in MIS upon completion of shift. Documentation should note that gas tank and dose levels were checked every four hours, usage of INOVent or INOPulse, mask or cannula, patient's tolerance, any troubleshooting necessary.
- 10.3 Study gas tank levels must be checked every four hours and documented on the CCTRCS check off sheet.
- 10.4 If any equipment breaks or is faulty, please tag and notify supervisor who will contact Gloria (6-0820) or Richard Cannon (6-9895).

11.0 REFERENCES

- 11.1 Datex-Ohmeda INOPulse Delivery System . Operation Manual
- 11.2 Critical Care and Respiratory Care Section. Nitric Oxide Therapy Policy
- 11.3 Y. Katayama, T. Higenbottam, G. Cremona, et al., University of Sheffield (UK). Minimizing the inhaled dose of NO with breath-by-breath delivery of spikes of concentrate gas.
- 11.4 J. Bates, University of Iowa College of Medicine. Inhaled Nitric Oxide: A selective pulmonary vasodilator.

SIGNATURE: _____ DATE: _____
Assistant Section Chief, CCTRCS, CCMD

SIGNATURE: _____ DATE: _____
Section Chief, CCTRCS, CCMD

SIGNATURE: _____ DATE: _____
Medical Director, CCTRCS, CCMD

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