Use of Nitric Oxide in Neonatal Transport

Inhaled Nitric Oxide Therapy for Near-Term Infants

Introduction

Inhaled Nitric Oxide (iNO) is an effective treatment for severe PPHN in babies approaching term who are at least 34 weeks gestation. It has been shown to reduce the incidence of death or referral for ECMO and current evidence suggests there is no neurodevelopmental disadvantage for survivors with iNO. Published evidence correlates with data from St Mary's Hospital suggesting that most babies who respond, do so immediately (approx 50% immediate sustained response with <10% additional infants showing a delayed benefit at SMH).

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator; it decreases pulmonary vascular resistance (PVR) thus reducing extra-pulmonary shunt. It also has a micro-selective effect which improves ventilation/perfusion matching. Early use of iNO can reduce FiO_2 and conventional ventilator requirements resulting in reduced secondary lung injury, mortality, need for ECMO, neurological sequelae and bronchopulmonary dysplasia. (NINOS, 1997)

The evidence of long-term benefit for preterm infants with PPHN is much weaker and thus an additional section of the guideline has been developed below.

Calculate OI from an indwelling arterial catheter:

OI = Mean Airway Pressure x Fio2 x 100 / PaO2 mmHg

Example:
baby on MAP 18, FiO2 0.95, PO2 2.0 kPa

Convert kPa to mmHg – 2.0 x 7.5 = 15

OI = 18 x 0.95 x 100/ 15
=114

Indications to commence inhaled Nitric Oxide:

An oxygenation index > 25 or persistent hypoxia despite maximal ventilation and

- Optimisation of airway and breathing manoeuvres
- Surfactant use where clinically indicated
- Optimisation of blood pressure and circulation
- Use of alkalinisation

If a cyanotic congenital heart malformation is strongly suggested by the clinical information then an urgent cardiological opinion should be sought. iNO should not normally be commenced in these infants.

All infants receiving iNO should also have a cardiological assessment within the next 24 hours or earlier if they fail to respond to treatment.

The Neonatal consultant must always be involved in the decision to commence iNO.

Commencing INO treatment

Commence treatment at 5 ppm and depending on response increase dosage by 5 ppm every 15 minutes to a maximum of 20 ppm.
At each step perform an arterial blood gas to recalculate OI. If at any step the OI falls below an absolute value of 10, then no further dose increase is required. A good response is defined as a reduction in OI from baseline by at least 20%. Such infants should be maintained on iNO for at least 12 hours.

If the infant has a reduction in OI < 20% compared to baseline values at 20 ppm, then this is deemed a treatment failure and the infant should commence rapid weaning of iNO. This should normally occur by a reduction of 5ppm every 15 minutes. There is normally no indication for dosages above 20 ppm except for a short term measure in infants who are awaiting transfer to an ECMO centre at their request.

Maintenance on iNO

Infants who have a continuing high OI (eg >50), or show no improvement, should be considered for transfer for ECMO rather than transfer to the original receiving Unit. This must be discussed with the Transport Consultant and receiving hospital Consultant.

The dose of iNO should be maintained at the optimal level as judged by the reduction in oxygenation index at each step. The infant should have continuous NO2 monitoring and once daily documentation of met-Hb levels. The need for iNO will be reviewed by the consultant on a twice daily basis, taking into account the disease process, ventilatory settings etc. In general once the ventilatory requirements are reducing and the OI falls to the range of 10 – 15 it will be appropriate to start reducing the iNO dose

Weaning from iNO

Initially the weaning of iNO should be commenced by steps of 5ppm every 4 hours until a dose of 5ppm is reached. Thereafter the baby should be weaned off at a rate of 1ppm every 2 hours with careful observations of oxygenation and calculations of the OI. If a worsening of OI or clinical condition occurs then further attempts at weaning may be deferred and occasionally the dose may need to be increased if there is a significant rebound effect. Rarely some infants will need very low dose therapy for up to 24 hours before tolerating complete withdrawal of iNO. Difficulties in withdrawing an infant from iNO should always be discussed with a consultant.

Inhaled Nitric Oxide for Preterm infants

The evidence base for the use of iNO in preterm infants is much weaker than for babies approaching or at term. A small number of patients may show a good response in the short term but it is unclear at present regarding long-term benefits of mortality and morbidity. The use of iNO may be justified in individual infants with severe pulmonary hypertension without other major complications who would otherwise be considered to have a good prognosis.

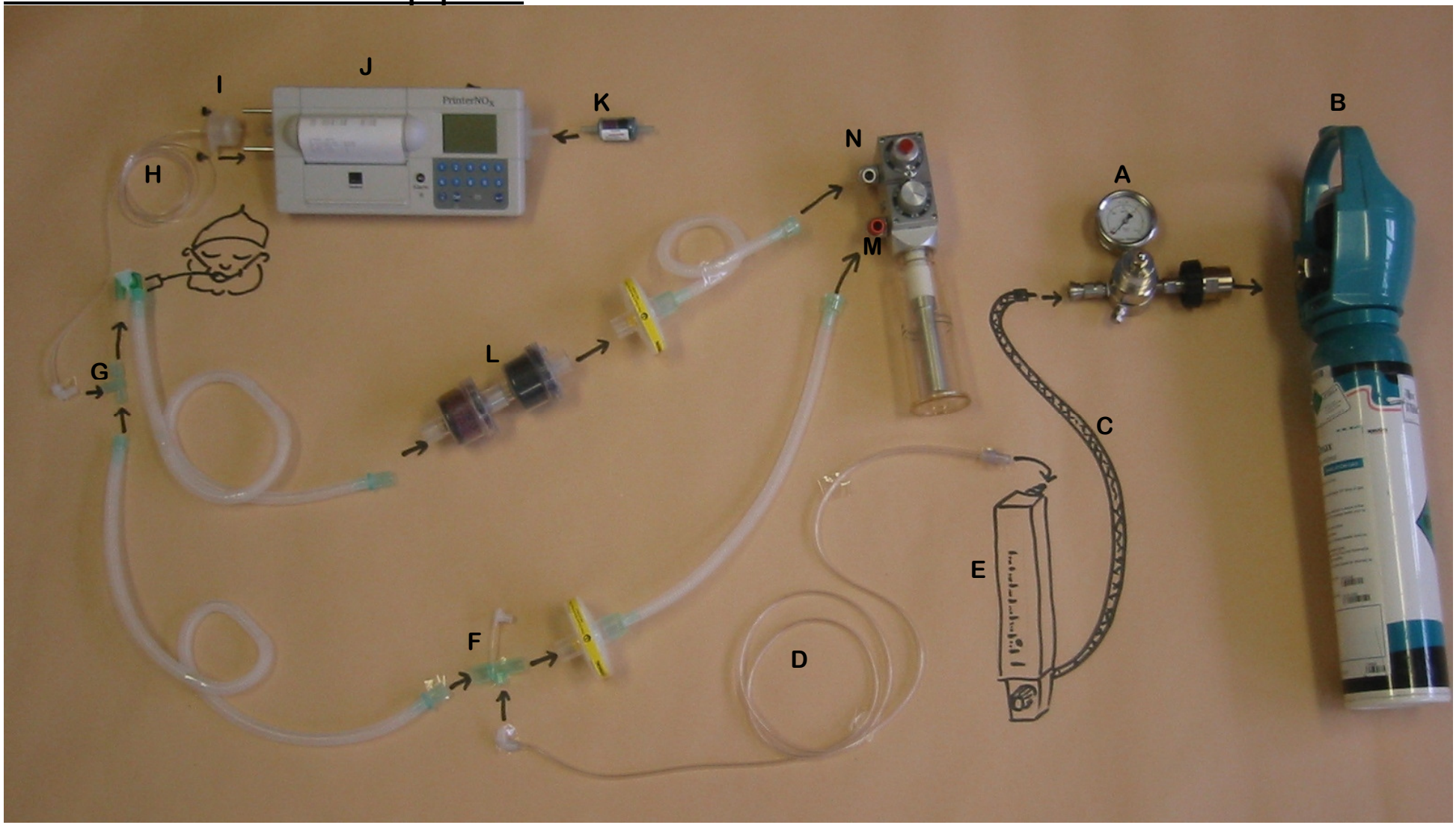
Any decision to commence iNO should be undertaken by a consultant having fully explored other treatment options such as surfactant therapy, correction of acidosis and hypotension, high frequency ventilation etc. It is recommended to assess the degree of pulmonary hypertension echocardiographically before commencing iNO as there is some evidence that this correlates with the likelihood of a good response. Infants thought to be below the margins of viability, greater than 28 days old, where the baby is moribund or where there are major concerns regarding brain injury should not normally treated with iNO.

The oxygenation criteria are the same as for Near Term babies (OI >25) but with echocardiographic evidence of severe pulmonary hypertension.

The process of initiation, maintenance and weaning of iNO are the same as for near term infants.

Neonatal Inhaled Nitric Oxide Study Group (1997) Inhaled Nitric Oxide in full term and nearly full-term infants with hypoxic respiratory failure. New England Journal of Medicine. 336. p597-604

The Nitric Oxide Circuit and Equipment

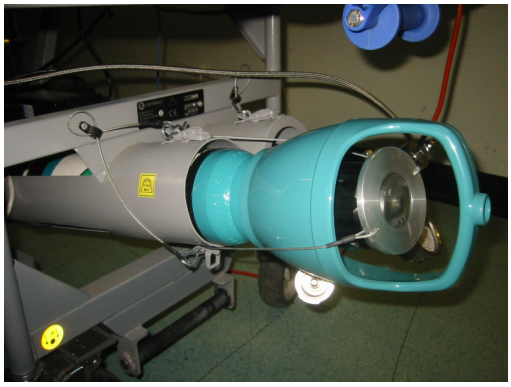


Equipment

- **B** - Nitric oxide cylinder (INO™ therapeutics) & **A** - regulator
- **E** - Flow meter with braided steel hose **C** to connect to cylinder
- Filtered circuit (including delivery line **D** & input port **F**, sampling port **G** & scavenger filters **L**)
- PrinterNOx monitor **J**, monitoring/sampling line **H** with H_2O trap **I**, PrinterNOx scavenger filter **K**

See photographs below for mounting/securing of Nitric Oxide cylinder, connection of circuit, scavenger filters and PrinterNOx monitor.

NO cylinder **B** with regulator **A** and steel-braided hose **C** attached



cylinder **B** secured in tube on trolley – retaining disc and wires must pass through the cylinder handle

showing position of NO cylinder B and flow meter E

Putting it all together – refer to photograph in previous section.

- Using Intersurgical ventilator circuit (ref 6362)
- Connect regulator **A** to Nitric Oxide cylinder **B**
- Plug steel-braided hose **C** into regulator **A** and secure cylinder in tube under trolley
- Nitric delivery line **D** connects to port on flow meter **E**
- Delivery line **D** connects via “elbow” to inlet port **F** in inspiratory limb – on patient side of filter
- Inspiratory limb NO sampling port **G** goes in inspiratory limb nearest to patient
- NO monitoring line **H,** including water trap **I,** goes from **G** to PrinterNOx **J**, secured by the two screws. The PrinterNOx monitor **J** is situated on top of the shelf on top of the incubator, to the left of the monitor (secured by Velcro)
- PrinterNOx scavenger filter **K** pushes in to outlet port – arrow indicates direction of gas flow
- In the expiratory limb of the circuit, connect large scavenger filters **L** before the circuit filter – the waste gases pass through pink granules first
- Inspiratory limb of circuit connects to red (inspiratory/Peak) port **M** on ventilator block (the bottom one)
- Expiratory limb of circuit connects to silver (expiratory/PEEP) port **N** on ventilator block (the top one)

How to Use

- Turn ventilator on and set flow to a total of 10L/min

- Set PEEP at 3cm H_2O to generate PEEP of 4-5cm H_2O, at a gas flow rate of 10L/minute of total flow. The scavenger filters in the expiratory limb cause back-pressure resulting in the need for lower set pressures to achieve desired PEEP This will result in an average PEEP level of 1.3cm H_2O more than is displayed on the ventilator
- Turn PrinterNOx on and select option 1 to access the measurement screen

- Turn NO cylinder on (+ and 3-digit timer display will appear)

- Set NO meter to desired flow, according to table below (**if** using a bias flow of 10L/min)

- On occasions you may require flow rates higher than 10 litres / min to achieve very high PIP settings. This will therefore require a greater flow of NO and use the cylinder more quickly.

NB - NO flow calculation is a rough guide and will need to be adjusted according to PrinterNOx readings obtained in option 7 from menu, i.e. if bias flow higher, NO flow meter will need to be set higher.

NITRIC OXIDE CONCENTRATION	NITRIC OXIDE FLOW METER RATE
5ppm	**130ml/min**
10ppm	**260ml/min**
15ppm	**390ml/min**
20ppm	**530ml/min**
25ppm	**670ml/min**

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Other useful general points:

- Set PEEP at 3cm H_2O to generate PEEP of 4-5cm H_2O, at a gas flow rate of 10L/minute of total flow.

- If the PrinterNOx displays “calibrate”, use it, but let the Technicians know ASAP

- 2000psi/138kpa = full cylinder

- At 20ppm there is a maximum 9 hours use per cylinder

- “-“ = off : ensure the “-“ is displayed (or we will be charged!)
  “+” = on
- The flow meter is marked in ml/minute, not Litres/minute
- The whole circuit (including circuit filters and large scavenger filters should be placed inside the incubator – the yellow ones across the foot of the “bed”, and the scavenger ones along the back)
- Do not over-tighten the flow meter when turning off – it breaks VERY easily

- The measurement on the flow meter is taken from the top of the bobbin/float, not the middle

Further information

Nitric Oxide Cylinders

These are kept in the technicians' room – a new cylinder should be used for each transfer, even if a minimal amount of gas was used. When the cylinder is not loaded in the transport incubator it is safer to lie it down on the floor. The regulator is kept in the transport equipment cupboard.

Although the cylinders are robust, it is calculated that if the entire contents of one cylinder discharged rapidly into an ambulance interior, the resulting concentration of Nitric Oxide would be less than 10 parts per million, which would therefore have no adverse effects on the crew or occupants of the ambulance.

Circuit

The green connectors for the inlet and monitoring/sampling ports and the delivery line are taken from the packs of lines & connectors used on NNMU nitric setup; there should be a supply of packs made up ready to assemble for transport Nitric use. These will be stored in the transport cupboard near the ventilator circuits

The "elbows" that connect the delivery & monitoring lines to the circuit come attached to the lines already.

The monitoring line and attached water trap, PrinterNOx scavenger filter, and the large circuit scavenger filters are **all single use** (as is the circuit).

PrinterNOx

Set alarm limits on PrinterNOx (option 3 on menu)

PrinterNOx has an internal battery which lasts around 6 hours however is connected to the inverter on the transport incubator and will charge continuously.

When setting the PrinterNOx to calculate the NO flow (no.7 on menu screen) the ventilator bias flow is the total L/min of gases going through the ventilator i.e. 10L/min, and the NO gas concentration in bottle is 400ppm (stated on the cylinder label). Then enter the required amount of NO (i.e. 5ppm)
The information you have input is displayed on the top 3 lines of the next screen, and the next line tells you the required NO flow for the flow meter in ***L/min***. the flow meter is in ml/min, so convert by multiplying by 1000 (e.g. 0.13L/min =130ml/min). Alternatively use the chart on previous page

Bag and Mask Circuit

It is possible to set up a bag and mask circuit with inhaled nitric oxide, however when using this no scavenging system or monitoring of nitric is possible, so this should only be used for short periods or emergency situations. It cannot be connected simultaneously with iNO through the ventilator circuit.

Within the miNO pack, you will find a Y- connector already attached to 2 long lengths of green oxygen tubing and one short length of oxygen tubing. Attach the short length to the oxygen inlet connector on the bag and one of the long lengths to the oxygen outlet on the front of the ventilator as you would normally connect a bag.

Picture of the Y connector with the short length of green oxygen tubing connected to the oxygen connector on the bag.

TURN ON THE OXYGEN FLOW TO APPROXIMATELY THE SAME TOTAL FLOW AS BEING DELIVERED VIA THE VENTILATOR (THE TOTAL OF AIR AND OXYGEN FLOWS). DO NOT CONNECT THE NITRIC SUPPLY UNTIL YOU HAVE TURNED ON THE OXYGEN. When you are ready to start bagging with nitric oxide, disconnect the clear plastic nitric delivery line from the nitric oxide flow meter and connect instead the remaining long green oxygen tubing leading to the Y connector. **DO NOT ADJUST THE FLOW RATE OF NITRIC OXIDE.**

Picture of the Nitric Oxide flow meter with disconnected clear plastic ventilator delivery line and attached to one of the long lengths of green tubing

This will deliver nitric oxide at approximately the same concentration as was previously being delivered through the ventilator. You will need to silence the alarm on the PrinterNox as this will not detect any nitric passing through the ventilator circuit.

When you are ready to return to the ventilator, disconnect the green oxygen tubing from the nitric flow meter and reconnect the clear plastic delivery line immediately. Remember to turn off the oxygen from the bag and mask circuit to prevent draining the cylinder.