

Nitric Oxide Usage in Neonates

Guideline Responsibilities and Authorisation

Department Responsible for Guideline	NICU
Document Facilitator Name	Lee Carpenter
Document Facilitator Title	Neonatal Nurse Practitioner
Document Owner Name	Dr Jutta van den Boom
Document Owner Title	Clinical Director
Target Audience	Consultants, Registrars, NNPs, CNSs, RNs
<p>Disclaimer: This document has been developed by Waikato District Health Board specifically for its own use. Use of this document and any reliance on the information contained therein by any third party is at their own risk and Waikato District Health Board assumes no responsibility whatsoever.</p>	

Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
3	Kathryn Thorn	2019	New template Full review
4	Lee Carpenter	2020	Added references, weaning flow diagram

Nitric Oxide Usage in Neonates

Contents

1	Overview	3
1.1	Background	3
1.2	Purpose	3
1.3	Scope	3
1.4	Patient / client group	3
1.5	Definitions	3
2	Clinical Management	4
2.1	Equipment	4
2.2	Indications for use	4
2.2.1	Entry Criteria	4
2.3	Commencement of inhaled Nitric Oxide	5
2.3.1	Ventilator	5
2.3.2	CPAP	5
2.4	Initiating treatment with inhaled nitric oxide	6
2.5	Monitoring	7
2.6	Weaning	8
2.7	Potential Complications	9
3	Audit	9
3.1	Indicators	9
4	Evidence base	9
4.1	Bibliography	9
4.2	Associated Documents	10

Nitric Oxide Usage in Neonates

1 Overview

1.1 Background

Nitric oxide (NO) is a potent vasodilator used to treat pulmonary hypertension. It is a gas that is given into the ventilator or CPAP circuit and is inactivated instantly in blood, by reacting with haemoglobin. Therefore, it produces rapid and localized effects on the pulmonary vasculature with presumed minimal action on the systemic vasculature or systemic blood pressure.

1.2 Purpose

This guideline describes the process to administer inhaled nitric oxide (iNO) either via conventional ventilator or CPAP.

1.3 Scope

Consultants, Registrars, NNPs, CNSs, & Registered Nurses

1.4 Patient / client group

- Neonates with symptomatic Persistent Pulmonary Hypertension of the Newborn (PPHN) – proven clinically (i.e. 20% differential in pre/postductal saturations, only in babies with known patent ductus arteriosus), or by point of care ultrasound/echocardiography
- Neonates with severe hypoxaemic respiratory failure (i.e. oxygenation index >20, PaO₂ <60 mmHg or <8kPa despite 100% FiO₂), caused by i.e. meconium aspiration/exposure, postoperative pulmonary hypertension.
- Used with caution in preterm infants with < 34 weeks GA, as rescue treatment for severe hypoxic respiratory failure on a case by case basis.

1.5 Definitions

CNS	Clinical Nurse Specialist
CPAP	Continuous Positive Airway Pressure
FiO₂	Fraction of inspired oxygen
iNO	Inhaled Nitric Oxide
IVH	Intravascular Haemorrhage
NNP	Neonatal Nurse Practitioner
NO	Nitric Oxide
NO₂	Nitrogen Dioxide
OI	Oxygenation Index

Nitric Oxide Usage in Neonates

PPHN	Persistent Pulmonary Hypertension of the Newborn
PVR	Pulmonary vascular resistance

2 Clinical Management

2.1 Equipment

- iNO delivery circuit set up guideline is available at:
J:\WomenChildren\NICU\Education\CheatSheets2020
Hard copy also on Inosys trolley and Cheat Sheet folders in Nursery 1 and 2.
- Spare equipment for setup of NO delivery circuit can be found in Technician NICU workroom

2.2 Indications for use

- PPHN
- Severe hypoxia (oxygenation index >20, PaO₂ <60 mmHg or <8kPa despite 100% FiO₂.)

<p>Oxygenation Index (OI)</p> $OI = \frac{\text{Mean Airway Pressure} \times FiO_2 \times 100}{PaO_2}$ <p>SSH OI calculator: see https://www.starship.org.nz/health-professionals/calculators/respiratory-indices-calculator/</p>

2.2.1 Entry Criteria

- Echocardiogram to exclude cyanotic (duct dependant) congenital heart disease
- Gestation >34 weeks. (In exceptional circumstances inhaled nitric oxide may be used in preterm infants <34 weeks as a rescue remedy but requires discussion with Consultant)
- Absence of lethal congenital malformation
- Careful consideration in presence of IVH (grade 2-4) or coagulopathy

Nitric Oxide Usage in Neonates

2.3 Commencement of inhaled Nitric Oxide

2.3.1 Ventilator

- Assemble equipment according to **iNO delivery circuit set up guideline** (available on shared drive as above)
- Use in-line suction catheter to avoid interruption of circuit.
- Optimise lung inflation: Efficacy of iNO is dependent on the degree of lung inflation (i.e. less effective if lung under-expanded).
- Do not turn off ventilator during procedures such as reintubation or hand bagging.

2.3.2 CPAP

- SMO decision to use iNO via CPAP
- Assemble equipment according to **iNO delivery circuit set up guideline** ([iNO delivery circuit set up guideline](#)).
- Cautiously discontinue any intravenous vasodilators if in use.

NOTE: Neopuff needs to be set up and connected to iNO supply, so it can be used immediately if manual IPPV is needed (Refer to [Nitric Oxide-Inhaled \(iNO\): Nursing Management in Newborn Intensive Care Unit \(NICU\)](#) procedure (4938))

Doc ID:	1553	Version:	03	Issue Date:	15 MAR 2021	Review Date:	15 MAR 2024
Facilitator Title:	Clinical Director			Department:	NICU		
IF THIS DOCUMENT IS PRINTED, IT IS VALID ONLY FOR THE DAY OF PRINTING							Page 5 of 10

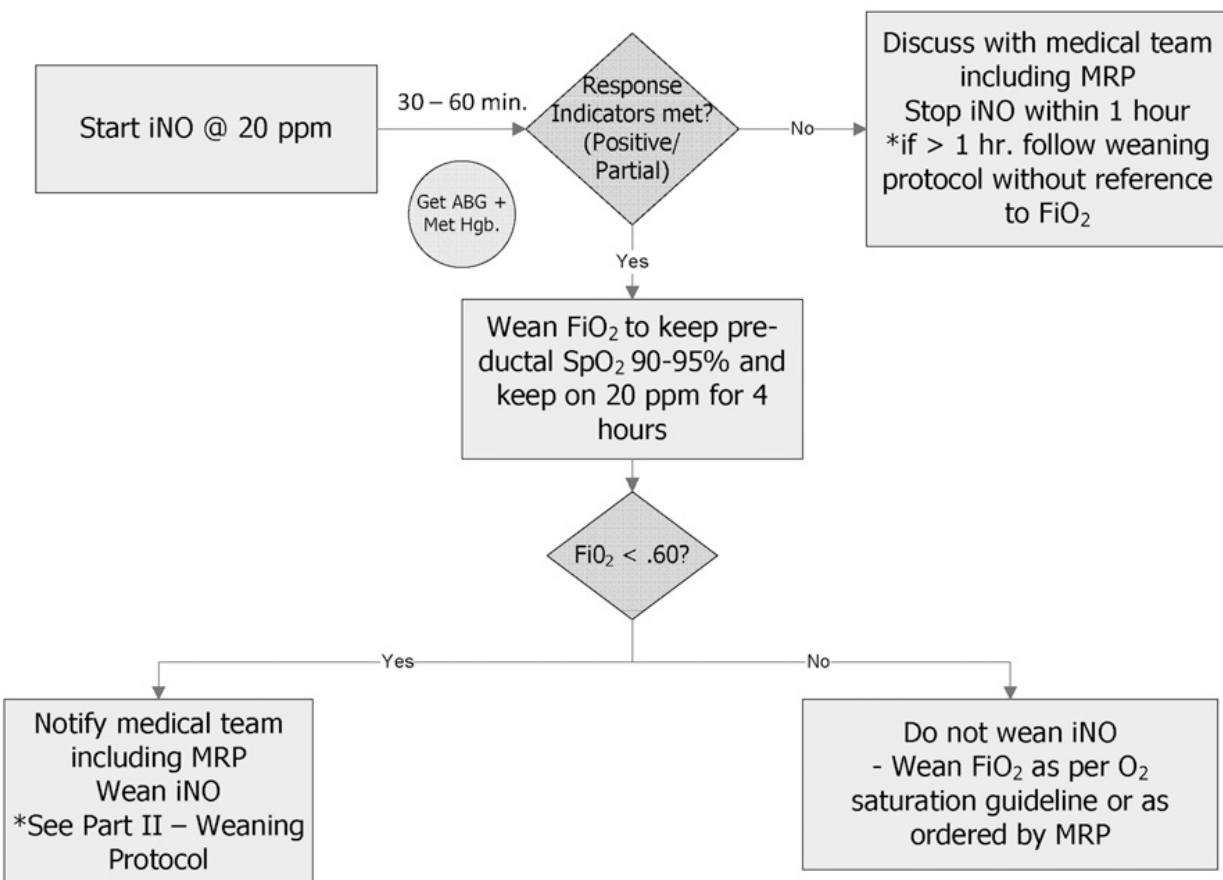
Nitric Oxide Usage in Neonates

2.4 Initiating treatment with inhaled nitric oxide

Indications for iNO
 PPHN or HRF or as indicated by echo
 O.I > 20 (consider at 15-20)

Ensure optimal lung recruitment (recent CXR to assess)

Obtain baseline vital signs and ABG



Response Indicators:

Positive

- ↑PaO₂ ≥ 20 mmHg
- ↑SpO₂ by 10%
- Or able to drop FiO₂ by at least 0.20

Partial

- ↑PaO₂ by 10 – 20 mmHg
- ↑SpO₂ by 5 – 10 %
- Or able to drop FiO₂ by at least 0.10 – 0.20

Methemoglobin (Normal < 2.5%)
 Obtain level is first ABG after starting iNO
 Obtain q24h thereafter

If Methemoglobin Hgb

- > 10% - Discontinue
- 5 – 10% Decrease iNO by 50% and repeat level
- < 2.5% Safe

Nitric Oxide Usage in Neonates

2.5 Monitoring

Continuous monitoring of heart rate, blood pressure and (arterial) oxygen saturation (refer [Oxygen Therapy for Newborns in NICU](#) protocol) with hourly documentation

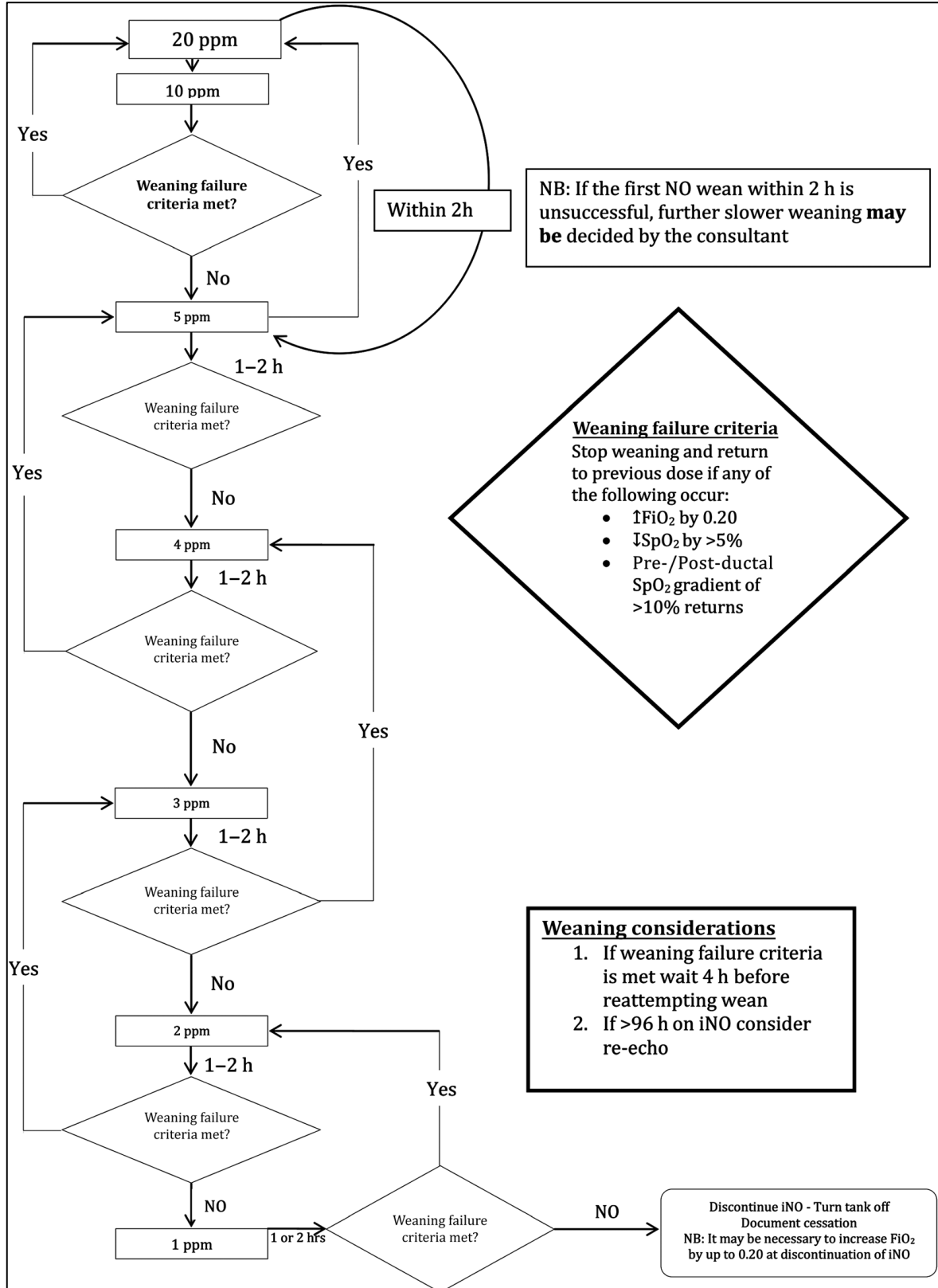
- OI calculation (see above) on arterial blood gases
- Pre and post ductal saturation monitoring
- Measure Methaemoglobin (from blood gas) after 1 hour and 12 hours (approximately) following commencement of iNO therapy to exclude methaemoglobin reductase deficiency. If methaemoglobin >5%, need to stop NO, inform SMO, and consider rescue therapy with methylene blue.
- Monitor Nitrogen Dioxide (NO₂) levels in inspiratory gases (upper limit 5ppm).

Doc ID:	1553	Version:	03	Issue Date:	15 MAR 2021	Review Date:	15 MAR 2024
Facilitator Title:	Clinical Director			Department:	NICU		
IF THIS DOCUMENT IS PRINTED, IT IS VALID ONLY FOR THE DAY OF PRINTING							Page 7 of 10

Nitric Oxide Usage in Neonates

2.6 Weaning

Exogenous iNO suppresses production of endogenous NO, therefore slow weaning, especially for the last few ppm is advised in order to avoid rebound PPHN.



Nitric Oxide Usage in Neonates

2.7 Potential Complications

1. Platelet dysfunction and bleeding
2. Methaemoglobinaemia (upper limit 5%)
3. Nitrogen Dioxide (NO₂) poisoning – pulmonary oedema, ARDS
4. Reduced FiO₂ in inspiratory gases due to displacement by NO (probably negligible)
5. Prevents pulmonary vascular bed remodelling (prolonged use in animal experiments)

NOTE: There are no restrictions for pregnant staff members to care for babies treated with iNO.

3 Audit

3.1 Indicators

- All neonates, receiving iNO, meet the entry criteria (2.2.1)
- All neonates commence iNO at 20ppm (unless contraindicated)
- Methaemoglobin levels are measured and documented in clinical notes at 1 hour and 12 hours after the commencement of iNO
- Documentation of OI in clinical notes

4 Evidence base

4.1 Bibliography

- Ahearn J., Panda M., Carlisle H., & Chaudhari T. Impact of inhaled nitric oxide stewardship programme in a neonatal intensive care unit. *Journal of Paediatrics and Child Health* 56 (2020) 265–271 © 2019 Paediatrics and Child Health Division (The Royal Australasian College of Physicians)
- P. Chandrashekhara et al. Early use of iNO in Preterm Infants. Is there a rationale for selective approach? *Am.J.Perinatol.* 2017 Apr 345(5):428-440
- M. Busè et al. Inhaled nitric oxide as a rescue therapy in a preterm neonate with severe pulmonary hypertension: a case report. *Ital J Pediatr.* 2018; 44: 55.
- Nitric oxide for respiratory failure in infants born at or near term. Finer N. and Barrington K Cochrane Library, 18.10.2006.
- Nitric oxide – inhaled. Retrieved April 18th 2020 from: <https://www.starship.org.nz/guidelines/nitric-oxide-inhaled>
- SSH OI calculator: see <https://www.starship.org.nz/health-professionals/calculators/respiratory-indices-calculator/>

Doc ID:	1553	Version:	03	Issue Date:	15 MAR 2021	Review Date:	15 MAR 2024
Facilitator Title:	Clinical Director			Department:	NICU		
IF THIS DOCUMENT IS PRINTED, IT IS VALID ONLY FOR THE DAY OF PRINTING							Page 9 of 10

Nitric Oxide Usage in Neonates

4.2 Associated Documents

- NICU Nursing procedure [Nitric Oxide-Inhaled \(iNO\): Nursing Management in Newborn Intensive Care Unit \(NICU\)](#) (4938)
- NICU Medical protocol [Oxygen Therapy for Newborns in NICU](#) (3115)

Doc ID:	1553	Version:	03	Issue Date:	15 MAR 2021	Review Date:	15 MAR 2024
Facilitator Title:	Clinical Director			Department:	NICU		
IF THIS DOCUMENT IS PRINTED, IT IS VALID ONLY FOR THE DAY OF PRINTING							Page 10 of 10