Inhaled Nitric Oxide For Treatment Of Hypoxic Respiratory Failure In Term/Near-Term Infant

*Eligibility Criteria*
1. GA ≥ 34 weeks
2. Diagnosis of HRF
3. ECHO to R/O CHD
4. Should already need:
   • ventilation ± HFV
   • O.I. ≥ 25

If eligibility criteria met, begin iNO at 20 PPM*

**Clinical Response**
1. Occur < 60 min.
2. Response include:
   • ↑ in PaO2 > 20 mmHg
   • 20% ↓ in O.I.

***Weaning Criteria***
1. FiO2 < 60%
2. PaO2 > 60 mmHg

Initial Clinical Response? **

Yes

1. Continue at 20 PPM until weaning criteria met***
2. Wean by 50% of start-up value or from 20 to 5 PPM within first 24H
3. Wean from 20 to 5 PPM in 5-PPM steps q 2-4H

Patient Stable at 5 PPM?

Yes

Patient Stable at 1 PPM?

Yes

Reduce in 1-2 PPM steps slowly from 5 to 1 PPM over 24-48H

No

Patient Stable at 1 PPM?

No

Patient Stable Off iNO?

Yes

Patient Stable Off iNO?

No

Trial Off

Patient Stable Off iNO?

Yes

STOP!
Inhaled Nitric Oxide For Treatment Of Hypoxic Respiratory Failure
In Term/Near-Term Infant

Hypoxic respiratory failure (HRF) or persistent pulmonary hypertension of the newborn (PPHN) are terms often used interchangeably. They refer to a clinical syndrome with a wide range of cardiac and pulmonary dysfunction with common pathophysiologic problems including: (1) sustained increase in pulmonary vascular resistance, (2) abnormal pulmonary vasoreactivity, and (3) severe systemic hypoxia.

Nitric oxide (NO) or endothelial-derived relaxing factor is a naturally occurring vasodilator produced by conversion of L-arginine in endothelial cells by endothelial nitric oxide synthetase (NOS). NO induces guanylate cyclase to increase cyclic guanosine monophosphate (cGMP), which reduces intracellular calcium and relaxes arteriolar smooth muscle by prohibiting myosin protein cross-bridge formation in smooth muscle. iNO has been shown to selectively relax pulmonary vascular smooth muscle with no adverse effect on the systemic vascular bed.

1. Infants with progressive hypoxic respiratory failure should be cared for in centers with the expertise and experience to provide multiple modes of ventilatory support and rescue therapies or be transferred in a timely manner to such an institution.
2. iNO therapy should be given using the indications, dosing, administration, and monitoring guidelines outlined on the product label (http://www.fda.gov). An echocardiogram to rule out congenital heart disease is recommended. Center-specific criteria for treatment failure should be developed to facilitate timely consideration of alternative therapies.
3. iNO therapy should be directed by physicians qualified by education and experience in its use and offered only at centers that are qualified to provide multisystem support, generally including on-site ECMO capability.
4. Generally, iNO should be initiated in centers with ECMO capability. If iNO is offered by a center without ECMO capability, for geographic or other compelling reasons, mutually acceptable treatment failure criteria and mechanisms for timely transfer of infants to a collaborating ECMO center should be established prospectively. Transfer must be accomplished without interruption of iNO therapy.
5. Centers that provide iNO therapy should provide comprehensive long-term medical and neurodevelopmental follow-up.
6. Centers that provide iNO therapy should establish prospective data collection for treatment time course, toxic effects, treatment failure, use of alternative therapies, and outcomes.
7. Administration of iNO for indications other than those approved by the FDA or in other neonatal populations, including compassionate use, remains experimental. As such, iNO should be administered according to a formal protocol that has been approved by the FDA and the institutional review board and with informed parental consent.

The protocol outlined is intended to help the provider determine the proper use of iNO therapy in the term and near-term infant with HRF, including eligibility criteria, start-up dosing, as well as criteria for weaning and stopping therapy.
References