

Pediatric Mechanical Ventilation with Nitric Oxide

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Since 1991, we have treated well over 600 patients with inhaled nitric oxide (INO) at Children's Hospital in Boston, MA. This technology has dramatically improved over the years. Initially, we administered nitric oxide (NO) via the double blender and a third gas source (nitrogen) technique, analyzed by a chemiluminescence device. This delivery system, although reliable, was labor intensive and cumbersome.

The titration method, employing the Bedfont Scientific NOxBOX gas analyzer, was later used. Now we have graduated to a much more simplified method of delivery, using the INO Therapeutics, Inc. INOvent. This device provides constant concentration, continuous monitoring, easy calibration, and is versatile with many ventilators in all modes.

Members of our respiratory care department have authored many articles for publications on the administration of INO.

Nitric oxide physiology

In healthy humans, nitric oxide regulates basal pulmonary vascular resistance (PVR) and helps to maintain a low PVR compared with the systemic vascular resistance.¹ NO is manufactured in small amounts in the human body. INO, as a potent and selective pulmonary vasodilator, is a new and encouraging therapy for newborn and pediatric pulmonary hypertension and respiratory failure. Primary respiratory failure in children is the most common pathway leading to cardiopulmonary arrest, which is a significant factor in morbidity and mortality in the pediatric inten-

sive care unit.^{2,3} By improving the ventilation-perfusion ratio inequalities and increasing arterial oxygenation, INO allows for weaning of harmful ventilatory support and decreases the need for extracorporeal membrane oxygenation (ECMO).^{3,4,5}

Nitric oxide is a colorless gas with a density similar to air. It is a known air pollutant resulting from the combustion of various substances such as fossil fuels.^{6,7} It is a highly diffusible endogenous molecule and has been identified as an important substance responsible for a number of bioregulatory functions. Systemic and pulmonary vascular tone is regulated by NO.

When NO is inhaled, it diffuses from the alveolar space into adjacent vascular smooth muscles and causes relaxation.^{8,9} The vasoactive effect of INO is

Main Component View



Figure 1. Front view of the INOvent.

confined to the pulmonary vasculature because NO binds with hemoglobin and is rapidly inactivated.¹ Therefore, systemic vasodilation is avoided and selective pulmonary vasodilation is achieved.^{8,9}

Clinical applications

The selective pulmonary dilation produced by INO has been used effectively in neonatal and pediatric patients for both diagnostic and therapeutic applications.^{2,7} In the newborn, when unoxygenated blood is shunted through a patent ductus arteriosus and/or the foramen ovale, increased PVR results in elevated pulmonary artery pressures. This leads to persistent pulmonary hypertension (PPHN). Meconium aspiration, respiratory distress syndrome, neonatal sepsis, congenital diaphragmatic hernia (CDH), and pneumonia can also cause PPHN.

As a selective pulmonary vasodilator, INO may reverse intrapulmonary shunting and restore normal circulation.⁶ Clinical studies show that INO effectively improves systemic

oxygenation without affecting systemic hemodynamics; it also reverses shunting. INO doses of 20 ppm or lower are effective. Weaning from mechanical ventilation seems to hasten after initiation of INO with PPHN patients. INO significantly reduces the need for ECMO in PPHN patients.²

Acute respiratory distress syndrome (ARDS) in children continues to be associated with a mortality rate as high as 70 percent.^{2,3,10,11} ARDS is characterized by an inefficient alveolar-capillary interface that leads to increased permeability and edema.^{3,10,11} Pulmonary circulation is constricted to varying degrees, which leads to pulmonary hypertension and right-sided heart failure, resulting in ventilation-perfusion mismatch and hypoxemia.

Treatment strategies have been aimed at enhancing the ventilation-perfusion relationship and have included recruitment of lung volume with positive end-expiratory pressure or high-frequency oscillating ventilation.² Although more clinical

trials are needed, low-dose INO (less than 10 ppm) with mechanical ventilation has been shown to improve gas exchange, increase PaO₂ (arterial oxygen tension), decrease PVR, and improve pulmonary artery pressures for pediatric ARDS patients. These results should allow for lower mechanical ventilator support and lessen its complications.³

INO and heart-lung transplantation

INO is used diagnostically in the cardiac catheterization lab to identify those patients with reversible pulmonary hypertension who are either a candidate for surgical repair or medical management. It is also used preoperatively to manage pulmonary hypertension for patients awaiting a heart or lung transplant.¹ Because INO is a selective pulmonary vasodilator, it promotes pulmonary vascular tone for heart and lung transplant patients. It can be used as a bridge to transplantation during surgery for hemodynamic stability and post-op for graft protection and preservation. During cardiac surgery, PVR is increased by cardiopulmonary bypass.¹ INO allows for stabilization of hemodynamics coming off bypass. In addition, INO is used post-operatively to manage pulmonary hypertension for cardiac surgery as well as heart or lung transplant patients.¹

Case report studies suggest that INO with moderate mechanical ventilation may be a useful adjunctive therapy in the stabilization of CDH patients in the perioperative period and may reduce the need for ECMO.

Circuit Connection Diagram

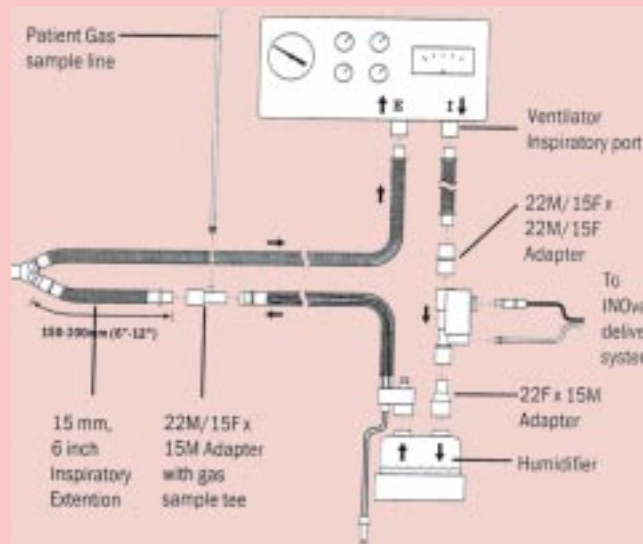


Figure 2. INOvent connected to a positive pressure ventilator.

It may also facilitate delayed surgical repair.²

NO delivery during mechanical ventilation

An ideal system should provide accurate and stable NO doses; minimize the production of nitrous oxide (NO₂); minimize contamination of the environment; monitor NO, NO₂, and O₂ concentrations continuously; and preserve mechanical ventilator function.^{2,7} The INOvent consists of an integrated delivery and monitoring system that delivers precise doses of NO gas by means of a specially designed injector module. The injector module measures and tracks inspiratory flow rate and proportionally delivers NO throughout the inspiratory phase during mechanical ventilation. (See Figure 1.)

The INOvent delivery system tracks ventilator waveforms and injects a synchronized and proportional flow rate of NO. This supplies a constant concentration of NO to the patient and can be

used with most ventilators in all modes.¹²

For infant, pediatric, and adult circuits, the injector module should be placed on the inlet of the humidifier. The arrow on the module should be in the direction of ventilator gas flow. A 22 mm/22 mm adapter is needed to make the

connection between module and humidifier inlet. The sample line adapter connects to the airway temperature port on the inspiratory limb. The sample flow-rate for gas analysis is 230 cc per minute. This flow rate is subtracted from the main gas flow and may affect flow trigger sensitivity. (See Figure 2).

For use with the SensorMedics 3100A, a one-way valve should be placed between the injector module and the humidifier inlet. This prevents the injector module from detecting expiratory gas flow. The sample line adapter is connected to the temperature port located between the green and blue mushroom valves. (See Figure 3.)

Manual ventilation with INO

Certain patients receiving INO therapy may not tolerate interruptions of NO delivery during procedures such as endotracheal suctioning or transport.^{6,7,13} In these situations, it is useful to have a manual ventila-

Connection to a High-Frequency Oscillatory Ventilator Circuit

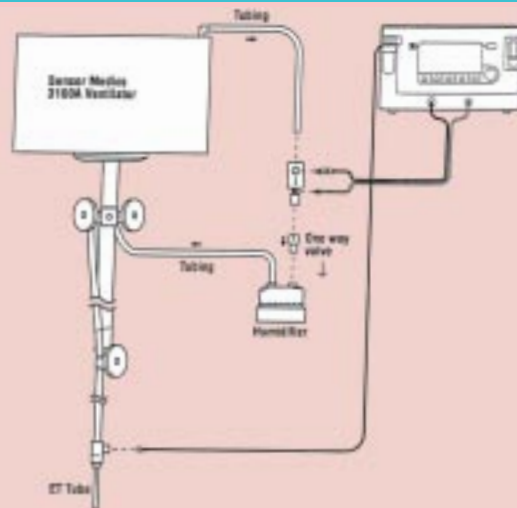


Figure 3. INOvent connected to a SensorMedics 3100A Ventilator.

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tion system that can supply stable NO concentrations.⁶ The INOvent can be used with self-inflating and non-self-inflating resuscitator bagging systems. It can also be used with spontaneous breathing circuits.

Adverse effects of INO

An awareness of potential toxic effects of INO is important when delivering NO either to the spontaneously breathing or mechanically ventilated patient. Toxic effects can include: an increased methemoglobin level, the formation of nitrogen

dioxide when NO reacts with oxygen,^{6,7,14} a prolonged bleeding time, and inhibition of platelet aggregation.^{1,14} INO may have a direct toxic effect on the lungs, resulting in damaged pulmonary surfactant, pulmonary edema, focal collapse, hyperinflation, and intra-alveolar hemorrhage.^{14,15} The extent of toxicity and adverse effects is difficult to quantify. It seems that lower INO doses, administered by clinicians familiar with its use, result in fewer toxic effects. The potential benefits must be balanced against the risks.¹⁴

Summary

The long-term effects of INO are not fully understood; however, the use of INO with the mechanically ventilated neonatal or pediatric patient in the critical care setting seems to be safe. An appreciation for the potential hazards and the development of accurate and safe delivery systems are paramount to the successful application of this relatively new therapy.⁶

The ability of INO to provide selective pulmonary vasodilation has become an important development in the clinical management of some cardiac and pulmonary disorders. By improving ventilation/perfusion and thus oxygenation, INO allows the use of lower mechanical ventilator support and results in fewer detrimental side effects. 🌊

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EDITOR'S NOTE

See the February and March 1999 issues of RESPIRATORY CARE Journal for in-depth coverage of the September 1998 AARC Journal Conference on inhaled nitric oxide.

See the "Tools of the Trade" column in this issue for additional resources on this topic.