SCIENCE AND TECHNOLOGY

Inhaled Nitric Oxide in the Operating Room

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ABSTRACT

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator increasingly used in the operating room to support patients with respiratory or cardiovascular compromise. Its ability to reduce pulmonary artery pressures without lowering systemic vascular resistance has made it a valuable therapy for pulmonary hypertension, right ventricular (RV) dysfunction, acute respiratory distress syndrome (ARDS), and procedures requiring one-lung ventilation. This article provides an overview of how nitric oxide works, the conditions in which it is most beneficial, and the precautions that must be taken during its administration. Through its highly targeted effects and ease of delivery via ventilator circuits, iNO has become an essential tool in perioperative care, especially in patients who have right heart dysfunction, pulmonary hypertension, or hypoxemia.

INTRODUCTION TO NITRIC OXIDE

Nitric oxide (NO) is a naturally occurring chemical mediator in the human body that plays a critical role in regulating blood flow. It functions by relaxing the smooth muscles within blood vessels, causing vasodilation, which allows them to widen and improve circulation. In medicine, this property is harnessed through the administration of inhaled nitric oxide, particularly in surgical and critical care settings. When administered via the respiratory tract, iNO acts directly on the pulmonary vasculature, relaxing blood vessels in the lungs without affecting those in the rest of the body. This precise and localized action is especially important in patients undergoing surgery, where fluctuations in blood pressure or oxygen

delivery can have serious consequences (Kamenshchikov et al., 2023).

MECHANISM OF ACTION

The therapeutic effects of iNO are rooted in its interaction with the cyclic guanosine monophosphate (cGMP) signaling pathway. Upon inhalation, nitric oxide diffuses across the alveolar-capillary membrane and binds to guanylate cyclase within the smooth muscle cells of the pulmonary vasculature. This interaction increases cGMP levels, which then promotes relaxation of the muscle tissue and subsequent vasodilation. As a result, blood is preferentially directed to areas of the lung that are well ventilated, improving ventilation/perfusion (V/Q) matching and enhancing overall oxygen uptake (Kamenshchikov et al., 2023).

CLINICAL INDICATIONS AND SURGICAL APPLICATIONS

Inhaled nitric oxide is commonly used in patients experiencing pulmonary hypertension or respiratory failure, especially during surgical procedures. Pulmonary hypertension is a serious condition in which the blood pressure within the arteries of the lungs becomes abnormally high. This elevation is often caused by chronic lung disease, congenital heart defects, or autoimmune disorders, and it forces the right side of the heart to work harder to push blood through the narrowed pulmonary vessels. Over time, this increased workload can weaken the right ventricle, potentially leading to right-sided heart failure. During surgery, especially when anesthesia and mechanical ventilation are involved, patients with pulmonary hypertension are at high risk for complications related to poor blood flow and oxygenation. In such cases, iNO reduces the pressure in the pulmonary arteries by dilating the vessels in the lungs, easing the burden on the heart and improving circulation (Kamenshchikov et al., 2023).

Another major indication for iNO is acute respiratory distress syndrome (ARDS), a life-threatening condition marked by widespread inflammation in the lungs, fluid accumulation in the alveoli, and severely impaired gas exchange. ARDS can occur in response to trauma, infection, or other systemic illnesses and often leads to significant hypoxemia (low oxygen levels in the blood) that is resistant to conventional oxygen therapy. In this context, iNO selectively increases blood flow to better-ventilated areas of the lung, thereby improving V/Q matching and enhancing oxygen delivery. Although iNO does not alter the underlying inflammation or resolve the disease itself, its ability to optimize oxygenation provides critical support while the patient recovers or undergoes surgical intervention (Kamenshchikov et al., 2023).

In addition to pulmonary hypertension and ARDS, iNO is frequently employed in thoracic surgeries such as lung transplants that require one-lung ventilation. During these procedures, one lung is deflated to give the surgeon better access to the chest cavity, while the other lung must provide all the gas exchange. iNO can enhance oxygenation by diverting blood flow away from the non-ventilated lung and toward the ventilated one, reducing shunt fraction (the amount of blood passing through the lungs without oxygenation) and preventing hypoxemia. This selective redirection of blood flow is critical for maintaining adequate oxygenation when pulmonary function is compromised. The use of iNO is also well established in patients with congenital heart defects or advanced lung disease awaiting transplantation, where careful control of pulmonary pressures is essential (Kamenshchikov et al., 2023; Muenster et al., 2024).

ADMINISTRATION AND MONITORING

Inhaled nitric oxide is administered through specialized delivery systems connected to the ventilator circuit, which is the tubing system that connects a mechanical ventilator to the patient's lungs. These systems precisely control the concentration of nitric oxide, typically in the range of 1 to 80 parts per million (ppm), with most institutions utilizing doses between 5 and 40 ppm for perioperative support (Muenster et al., 2024). Due to its gaseous form, the drug is delivered directly to the lungs, where it begins to act almost immediately. However, the administration of iNO requires vigilant monitoring to ensure efficacy and prevent complications.

Two of the most concerning adverse effects are methemoglobinemia and nitrogen dioxide (NO_2) toxicity. Methemoglobinemia occurs when nitric oxide oxidizes hemoglobin, reducing its ability to carry oxygen. Regular blood tests are performed to monitor methemoglobin levels and ensure they remain within safe limits. NO_2, a byproduct of nitric oxide interacting with oxygen, can irritate the lungs and airways if allowed to accumulate. Modern delivery systems are equipped with sensors to continuously measure NO and NO_2 concentrations, helping prevent exposure to harmful levels. Another important consideration is the risk of rebound pulmonary hypertension, which can occur if iNO is withdrawn too quickly. To avoid this, the dosage is gradually tapered while monitoring the patient's hemodynamic stability, a state of healthy and stable blood circulation (Muenster et al., 2024).

PERIOPERATIVE CONSIDERATIONS

Successful use of inhaled nitric oxide in the operating room requires coordination among the anesthesia team and respiratory therapists. The timing of initiation depends on the patient's condition; in some cases, iNO is started before the induction of anesthesia, especially if the patient has

known pulmonary hypertension or right heart failure. In other situations, it may be introduced intraoperatively if signs of increased pulmonary pressures or hypoxemia develop. The anesthesia machine must be compatible with the nitric oxide delivery system, and all equipment must be carefully calibrated before use (Gille et al., 2012).

Monitoring iNO includes frequent arterial blood gas analyses, methemoglobin levels, and invasive measurements of pulmonary artery pressures in select patients. Transesophageal echocardiography is often used to assess the right ventricular function and guide fluid and vasopressor management. Additionally, transport of patients receiving iNO requires mobile tanks, backup delivery systems, and careful coordination to ensure uninterrupted therapy during intra-hospital transfers. Despite its effectiveness, iNO is associated with a high cost compared to alternatives such as inhaled epoprostenol, an aerosolized vasodilator (prostacyclin analogue). Cost-effectiveness must be considered when selecting therapy, particularly in resource-limited settings or when long-term use is anticipated (Gille et al., 2012; Muenster et al., 2024).

NITRIC OXIDE IN CARDIAC SURGERY

The use of inhaled nitric oxide is especially prominent in the context of cardiac surgery, particularly in patients with pulmonary hypertension undergoing procedures such as valve replacements or congenital heart defect repairs. These patients often have elevated pulmonary pressures that can compromise right ventricular function, making surgical intervention more precarious. In such cases, iNO serves to reduce pulmonary vascular resistance, thereby easing the burden on the right ventricle and improving hemodynamic stability during and after the procedure (Kamenshchikov et al., 2023).

One of the most critical moments in cardiac surgery is separation from cardiopulmonary bypass (CPB), a point at which the heart must resume effective circulation on its own. In patients with pulmonary hypertension, this transition can be challenging due to the high resistance the right ventricle must overcome. iNO can facilitate smoother separation from CPB by lowering the resistance, known as afterload, that the right side of the heart must pump against in the pulmonary circulation. This reduction in pressure allows the heart to function more effectively without the continued support of the bypass machine. Moreover, iNO is often used after surgery when medications called inotropic agents, which help the heart pump more strongly, are insufficient to maintain right ventricular output. Its targeted vasodilatory effect improves oxygenation and cardiac output while avoiding systemic hypotension, a balance that is particularly important in the immediate post-CPB period (Kamenshchikov et al., 2023; Muenster et al., 2024).

CONCLUSION

Inhaled nitric oxide represents a remarkable advancement in the targeted management of pulmonary vascular disease in surgical patients. Its rapid onset of action, lung-specific vasodilation, and minimal systemic side effects make it an invaluable tool in the operating room, especially for patients with challenging cardiopulmonary conditions. While its use demands precise monitoring and specialized equipment, the clinical benefits of improved oxygenation and reduced right ventricular strain are worth the effort. As research continues to refine best practices and cost-effective alternatives, iNO remains a cornerstone therapy in the perioperative management of complex cases involving the heart and lungs.

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1. What is the primary benefit of inhaled nitric oxide (iNO) during one-lung ventilation?
A) Increases cardiac preload
B) Enhances systemic blood pressure
C) Improves ventilation-perfusion matching
D) Reduces carbon dioxide retention

2. What is the primary signaling pathway activated by inhaled nitric oxide in pulmonary smooth muscle cells?
A) Adenosine monophosphate (AMP)
B) Renin-angiotensin system
C) Cyclic guanosine monophosphate (cGMP)
D) Beta-adrenergic receptor cascade

3. Which complication is associated with sudden withdrawal of inhaled nitric oxide?
A) Metabolic acidosis
B) Rebound pulmonary hypertension
C) Arrhythmia
D) Hypoglycemia

4. What is the main reason iNO is preferred over systemic vasodilators during surgery?
A) It increases cardiac contractility to elevate heart rate
B) It acts only on the brain
C) It selectively dilates pulmonary vessels without lowering systemic blood pressure
D) It decreases respiratory drive to increase inspiration in patient

5. In which of the following conditions is inhaled nitric oxide most commonly used?
A) Chronic kidney disease
B) Pulmonary hypertension
C) Coronary artery disease
D) Aortic dissection

6. Which of the following is a safety measure used to prevent complications during iNO administration?
A) Delivering iNO without monitoring systems
B) Rapidly discontinuing therapy without tapering
C) Gradual dose reduction and real-time gas monitoring
D) Avoiding blood tests during treatment

7. True or False: Inhaled nitric oxide directly treats the inflammation caused by ARDS.
A) True
B) False

8. What role does iNO play during cardiac surgery, especially in patients coming off cardiopulmonary bypass (CPB)?
A) Increases afterload
B) Decreases systemic resistance
C) Reduces pulmonary vascular resistance
D) Increases myocardial oxygen demand

9. Which team members must be coordinated to ensure safe and effective iNO delivery during surgery?
A) Laboratory technicians only
B) Anesthesia team and surgical residents
C) Respiratory therapists and anesthesia team
D) Dietitians and case managers

10. True or False: iNO acts systemically to dilate blood vessels throughout the entire body.
A) True
B) False

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