

Richard B. Weiskopf, M.D., Editor

The following correspondence refers to a previously published Clinical Concepts and Commentary article by Haddad *et al.* (Haddad E, Lowson SM, Johns RA, Rich GF: Use of inhaled nitric oxide perioperatively and in intensive care patients. ANESTHESIOLOGY 2000; 92:1821-5).

Anesthesiology 2001; 94:354

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Is There a Place for Inhaled Nitric Oxide in the Therapy of Massive Pulmonary Embolism?

To the Editor:—Dr. Haddad *et al.*¹ have written an interesting and informative article regarding the beneficial effects of inhaled nitric oxide (inhaled NO) in perioperative and critical care patients. They believe that inhaled NO causes vasodilation that is proportional to the pulmonary vascular resistance in the presence of pulmonary vasoconstriction. Moreover, they have indicated that the effects of inhaled NO on cardiac function are dependent on the degree of right ventricular dysfunction.¹ We would like to mention recent evidence supporting the idea of using inhaled NO in the therapy of massive pulmonary embolism.²⁻⁴ Selective pulmonary vasodilator therapy with inhaled NO can attenuate effectively the pulmonary vasoconstriction caused by active mediators, such as endothelin-1^{5,6} and thromboxane A₂,^{4,6} which have been implicated in the pulmonary vasoconstriction and cardiodepression seen in pulmonary embolism. Indeed, inhaled NO blunted thromboxane A₂ release,⁴ lowered pulmonary artery pressure, and increased cardiac output after massive air embolism in dogs² and in four cases of pulmonary embolism.³ Although extrapolating these findings to the clinical situation is still a matter of debate, we believe that these recent findings support the use of inhaled NO during pulmonary embolism. Finally, it is possible to discontinue administration of inhaled NO if anything untoward happens.

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Anesthesiology 2001; 94:354

In Reply:—We presented a brief overview of the perioperative uses of inhaled nitric oxide (NO). Although we covered the most common indications for inhaled NO, the letter by Tanus-Santos correctly suggests that additional uses have been described, such as the management of pulmonary embolism. There are also case reports of the use of inhaled NO in hepato-pulmonary syndrome and after heparin-protamine reactions. Since the publication of our article, inhaled NO has received Food and Drug Administration approval for term and near-term (older than 34 weeks) neonates with hypoxic respiratory failure

References

1. Haddad E, Lowson SM, Johns RA, Rich GF: Use of inhaled nitric oxide perioperatively and in intensive care patients. ANESTHESIOLOGY 2000; 92:1821-5
2. Tanus-Santos JE, Moreno H Jr, Zappellini A, de Nucci G: Small-dose inhaled nitric oxide attenuates hemodynamic changes after pulmonary air embolism in dogs. Anesth Analg 1999; 88:1025-9
3. Capellier G, Jacques T, Balvay P, Blasco G, Belle E, Barale F: Inhaled nitric oxide in patients with pulmonary embolism. Intensive Care Med 1997; 23:1089-92
4. Tanus-Santos JE, Moreno H Jr, Moreno RA, Martins ML, Pereira R, de Nucci G: Inhaled nitric oxide improves hemodynamics during a venous air infusion (VAI) in dogs. Intensive Care Med 1999; 25:983-9
5. Dschietzig T, Laule M, Alexiou K, Schror K, Baumann G, Stangl K: Coronary constriction and consequent cardiodepression in pulmonary embolism are mediated by pulmonary big endothelin and enhanced in early endothelial dysfunction. Crit Care Med 1998; 26:510-7
6. Tanus-Santos JE, Gordo WM, Udelsmann A, Cittadino MH, Moreno H Jr: Nonselective endothelin-receptor antagonism attenuates hemodynamic changes after massive pulmonary air embolism in dogs. Chest 2000; 118:175-9

(Accepted for publication November 10, 2000.)

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associated with pulmonary hypertension. It is important to realize that all other uses of inhaled NO are considered "off-label." Furthermore, consideration of the use of inhaled NO to treat pulmonary hypertension with or without hypoxemia should include its considerable cost.

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(Accepted for publication November 10, 2000.)