

Combining Medical Gases in the Treatment of Pulmonary Interstitial Emphysema: Novel, Yes: But Is It Safe?

Helium-oxygen mixture (heliox) has been used with some success in the treatment of severe airflow obstruction associated with upper and lower airway abnormalities in infants and children.¹ *RESPIRATORY CARE*, in the special June 2006 issue, provided a thoughtful review of the clinical application of heliox and its associated technical challenges.² Inhaled nitric oxide (INO) has also been an important advancement and is considered safe in the treatment of pulmonary hypertension in newborns³ and slows the progression of chronic lung disease in premature infants.^{4,5} In this issue of *RESPIRATORY CARE*, Phatak and colleagues⁶ present an interesting case in which they combined heliox and INO in the management of an infant with severe pulmonary interstitial emphysema, which is an infrequent but difficult to manage complication of mechanical ventilation in preterm infants.

SEE THE CASE REPORT ON PAGE 1731

Though the infant ultimately did well, several technical issues should be pondered. Phatak et al used the Dräger Babylog ventilator in the volume-guarantee mode, which targets expiratory tidal volume (V_T) measurements made by a proximal hot-wire flow sensor. As the time constant changes, maximum inspiratory pressure auto-regulates within a predetermined limit to assure a given V_T (in this case 4–5 mL/kg). Heliox has cooling properties and can adversely affect a hot-wire flow sensor and cause overestimation of V_T , which would cause the inspiratory pressure to be titrated too low, which could increase the under-ventilation.⁷⁻⁹ Presumably to address that issue, Phatak et al also measured V_T with a secondary monitor (CO₂SMO Plus) that uses a pressure-differential flow sensor, which they calibrated for the presence of heliox. What is not clear is if the volume-guarantee option was switched off or if the secondary flow sensor was coupled with the ventilator flow sensor, in which case what volume was being targeted? Was the difference between the 2 monitoring devices estimated and the ventilator volume target adjusted accordingly? Following the addition of heliox, the maximum inspiratory pressure “dropped immediately” from 38 cm H₂O to 29 cm H₂O, which is a striking reduction, but, again, what volume target was being used? There was increased CO₂ retention at that point, and the

mandatory rate had been increased to 50 breaths/min. Since there was an increase in P_{CO_2} , there must have been a change in minute ventilation, so the effect of heliox alone could not have been fully evaluated.

Another technical matter was the “leak in hose system” ventilator alarm, which occurred when the heliox flow exceeded 12 L/min. That alarm signals a leak in the circuit or an over-shoot of the target pressure.¹⁰ The heliox flow they added seems excessive, which is probably why that alarm sounded. It is unclear why they used such a high heliox flow or what was the native ventilator continuous flow rate. Such a high flow could also lead to fairly turbulent flow in both the inspiratory and expiratory limbs, particularly in a small-diameter infant ventilator circuit. Also, if standard O₂ flow meters were used, was the difference in density factored in when reporting the flows?

In general, with heliox the goal is to deliver as close to an 80% helium/20% oxygen mixture as possible to maximize the density reduction and thus improve the flow and enhance CO₂ diffusion.¹¹ Though the application of heliox in this case was not specifically to overcome a flow problem, the maximum fraction of inspired helium (based on the reported fraction of inspired oxygen [F_{IO_2}]) was about 40%, which would have yielded only a small density reduction. Simply injecting 10–12 L/min of an 80% helium/20% oxygen mixture into the ventilator does not afford the maximum possible helium concentration. Although if the ventilator F_{IO_2} was set to 1.0, which would eliminate the presence of nitrogen, and at a very low flow rate, the heliox flow would have been the principle flow, but, again, the maximum helium concentration would still have only been about 40%.

Another point to consider is that calibrating the CO₂SMO Plus monitor for the presence of helium requires the clinician to input the exact helium concentration, to ensure measurement accuracy. If 80% helium was initially programmed into the monitor, the volume measurements would not have been accurate, because the actual highest helium fraction would have been only about 40%. More recent ventilator technology allows the air source to be replaced with a heliox source, which eliminates the presence of nitrogen.

The next technical point to contemplate is the addition of INO in combination with the heliox. The fundamental question is, is that safe? Very little is known about the interaction of helium and nitric oxide, or, for that matter, nitrogen dioxide. Phatak et al acknowledge that the available data about the safety of combining medical gases are limited. It appears that Phatak et al adapted the INO to the ventilator in a fairly standard fashion, with the injector module placed prior to the humidifier, and the sample line close to the patient airway. We do not know how the monitoring and gas-delivery mechanisms of the INO system they used behave in the presence of heliox, and a ventilator flow of at least 4 L/min is required for injector-module accuracy. Again, what ventilator flow was used? They provide little information about the INO dosing sequence, whether there were any discrepancies between the set and the measured fraction of helium, or the NO₂ level.

Phatak et al suggest that heliox may have improved the diffusion of INO. This is certainly an intriguing notion and a referenced point in this case,¹² but the physiology is not well understood. Judging by the changes in P_{O₂} and modest reduction in F_{I_{O₂}}, it appears that INO did not play a significant role in improving oxygenation. Also, heliox works primarily by reducing turbulence in the larger airways, and less so in the smaller airways, in which the flow is characteristically laminar, by virtue of the smaller airways' extensive branching,¹¹ and pulmonary interstitial emphysema typically develops in the terminal bronchioles.

Phatak et al faced the challenge of supporting gas exchange while trying to halt the progression of unilateral pulmonary interstitial emphysema, which could have led to further lung injury and morbidity. When faced with dilemmas in critical care, how far should the care team go? A delicate balance exists between adopting innovation on the fly and preserving safety. Respiratory therapists often find themselves at the crossroads of innovation and safety, and in the current health-care climate, safety tends to supersede innovation. In a thoughtful article by Rubin and Steinberg, in the April 2007 issue of *RESPIRATORY CARE*, these very points were well discussed.¹³ Evidence-based practice is often touted, but it is highly unlikely that we will ever see this level of exploration of heliox or heliox plus INO for pulmonary interstitial emphysema. Without

complete data we have to rely on judgment and the available information. At a minimum we need a "second set of eyes," a concerted team approach that includes the patient's parents and family members, a clear understanding of the risks, and agreed-upon end points.

Though Phatak et al suggest that heliox and INO were key in their patient's recovery, perhaps a more systematic approach to the 3 main interventions in this case (steroids, heliox, and then heliox plus INO) could have better determined what really worked and what did not. We must be cautious when employing the "everything-but-the-kitchen-sink" approach.

Peter Betit RRT-NPS FAARC
Department of Respiratory Care
Children's Hospital Boston
Harvard Medical School
Boston, Massachusetts

REFERENCES

1. Myers TR. Use of heliox in children. *Respir Care* 2006;51(6):619-631.
2. Fink JB. Heliox therapy: practice, evidence, risk, and opportunities. *Respir Care* 2006;51(6):607-660.
3. Barrington KJ, Finer NN. Inhaled nitric oxide for preterm infants: a systematic review. *Pediatrics* 2007;120(5):1088-1099.
4. Ballard RA, Truog WE, Cnaan A, Martin RJ, Ballard PL, Merrill JD, et al. Inhaled nitric oxide in preterm infants undergoing mechanical ventilation. *N Engl J Med* 2006;355(4):343-353.
5. Kinsella JP, Cutter GR, Walsh WF, Gerstmann DR, Bose CL, Hart C, et al. Early inhaled nitric oxide therapy in premature newborns with respiratory failure. *N Engl J Med* 2006;355(4):354-364.
6. Phatak RS, Pairaudeau CF, Smith CJ, Pairaudeau PW, Klonin H. Heliox with inhaled nitric oxide: a novel strategy for severe localized interstitial pulmonary emphysema in preterm neonatal ventilation. *Respir Care* 2008;53(12):1731-1738.
7. Brown MK, Willms DC. A laboratory evaluation of 2 mechanical ventilators in the presence of helium-oxygen mixtures. *Respir Care* 2005;50(3):354-360.
8. Oppenheim-Eden A, Cohen Y, Weissman C, Reuven P. The effect of helium on ventilator performance: study of five ventilators and a bedside pitot tube spirometer. *Chest* 2001;120(2):582-588.
9. Venkataraman ST. Heliox during mechanical ventilation. *Respir Care* 2006;51(6):632-639.
10. Babylog 8000Plus infant care ventilator operating instructions. Dräger Medical, Telford, PA; 1997.
11. Hess DR, Fink JB, Venkataraman ST, Kim IN, Myers TR, Tano BD. The history and physics of heliox. *Respir Care* 2006;51(6):608-612.
12. Petros AJ, Tulloh RM, Wheatley E. Heli-NO: enhanced gas exchange with nitric oxide in helium. *Anesth Analg* 1996;83(4):888-889.
13. Rubin BK, Steinberg KP. When caring for critically ill patients, do clinicians have a responsibility to be innovative and try unproven approaches when accepted approaches are failing? *Respir Care* 2007; 52(4):408-413; discussion 413-415.

The author reports no conflicts of interest related to the content of this editorial.

Correspondence: Peter Betit RRT-NPS FAARC, Respiratory Care Department, MA-861, Children's Hospital Boston, 300 Longwood Avenue, Boston MA 02115. E-mail: peter.betit@childrens.harvard.edu.