Use of Heliox Delivered via High-Flow Nasal Cannula to Treat an Infant With Coronavirus-Related Respiratory Infection and Severe Acute Air-Flow Obstruction

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Heliox, a helium-oxygen gas mixture, has been used for many decades to treat obstructive pulmonary disease. The lower density and higher viscosity of heliox relative to nitrogen-oxygen mixtures can significantly reduce airway resistance when an anatomic upper air-flow obstruction is present and gas flow is turbulent. Clinically, heliox can decrease airway resistance in acute asthma in adults and children and in COPD. Heliox may also enhance the bronchodilating effects of β-agonist administration for acute asthma. Respiratory syndromes caused by coronavirus infections in humans range in severity from the common cold to severe acute respiratory syndrome associated with human coronavirus OC43 and other viral strains. In infants, coronavirus infection can cause bronchitis, bronchiolitis, and pneumonia in variable combinations and can produce enough air-flow obstruction to cause respiratory failure. We describe a case of coronavirus OC43 infection in an infant with severe acute respiratory distress treated with heliox inhalation to avoid intubation. *Key words: heliox; high-flow nasal cannula; coronavirus; air-flow obstruction; respiratory syndrome.* [Respir Care 2014;59(11):e166–e170. © 2014 Daedalus Enterprises]

Introduction

Heliox, a helium-oxygen gas mixture, has been used for many decades in the management of obstructive pulmonary disease.[1] The lower density and higher viscosity of heliox relative to nitrogen-oxygen mixtures can significantly reduce airway resistance (R_{aw}) when an anatomic air-flow obstruction is present and gas flow is turbulent.[2,3] Heliox also reduces R_{aw} in acute asthma in adults and children and in adults with COPD exacerbations.[3-5] Heliox may enhance the bronchodilating effects of β-agonist administration for acute asthma.

Respiratory syndromes caused by coronavirus infections in humans range in severity from the common cold to severe acute respiratory syndrome associated with human coronavirus (HCoV) and other viral strains. In infants, coronavirus infection can cause bronchitis, bronchiolitis, and pneumonia in variable combinations and can produce enough air-flow obstruction to cause respiratory failure.[6,7] We describe a case of coronavirus OC43 infection in an infant with severe acute respiratory distress treated with

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heliox inhalation via high-flow nasal cannula (HFNC) to avoid intubation.

Case Report

A 10-month-old Hispanic male with a history of seizures was intubated in the field during a seizure and transported to the pediatric emergency department in Comer Children's Hospital at The University of Chicago. The patient was admitted to the pediatric ICU for ventilator management and started on anti-seizure medications. A chest radiograph was notable for left lower lobe opacity consistent with atelectasis or pneumonia. Over the next 2 d, the patient's seizures were controlled, and he was extubated and placed on HFNC (pediatric oxygen therapy nasal cannula, BC3780) for use with the RT329 system (Fisher & Paykel Healthcare, Auckland, New Zealand) at 5 L/min targeting an F_{IO_2} of 1.0. Upon admission, nasal swab respiratory viral testing was positive for coronavirus OC43. The microbiology viral panel methodology used to identify coronavirus OC43 in this case was polymerase chain reaction.

The patient's treatment plan immediately after extubation included handheld nebulizer treatments every 2 h with 0.083% albuterol via face mask and chest physical therapy every 2 h. The patient had no wheezing or stridor, but had coarse diminished breath sounds before and after the treatments. He had intermittent fevers, suprasternal chest retractions graded as + 5 using the pediatric advanced life support scale,[8] and nasal flaring both before and after handheld nebulizer and chest physical therapy treatments. The nebulizer was switched from a jet nebulizer to a vibrating mesh nebulizer (Aeroneb, Aerogen, Mountain View, California) in line with HFNC as described previously.[9]

Despite the intense respiratory care treatment regimen, the patient remained in severe acute respiratory distress. He developed tachypnea of 60–70 breaths/min with continued prominent chest wall retractions 24 h postextubation. In addition, he experienced periods of arterial desaturation to 80% by pulse oximetry. Inhaled β-agonist treatments were continued, and intravenous corticosteroids were administered.

The pediatric ICU team became concerned that the patient was depleting his respiratory muscle reserve due to increased work of breathing with persistent air-flow obstruction and was beginning to exhibit frequent periods of arterial oxygen desaturation. The arterial desaturations occurred despite HFNC at an F_{IO_2} of 1.0. More aggressive respiratory support options such as infant nasal CPAP, bi-level positive airway pressure, and re-intubation were considered. Because patients with air-flow obstruction can be very difficult to manage on mechanical ventilation,[10] a trial of heliox via HFNC was attempted to reduce R_{aw} and possibly prevent re-intubation.

Fig. 1. Setup for delivering heliox via high-flow nasal cannula. The heliox tank is on the right.

For heliox administration to be effective, the helium concentration must ideally be $\geq$ 60%, and gas flows must meet or exceed the inspiratory flow demands of the patient so that heliox concentration is not diluted with room air. Heliox is usually administered via a semiclosed non-rebreather mask. However, keeping a mask on an infant in severe acute respiratory distress can be difficult. We administered heliox (Airgas Puritan Medical, Radnor, Pennsylvania) via HFNC utilizing the RT329 system, which was connected to the gas inlet side of the humidifier chamber (Fig. 1). The primary gas source for HFNC consisted of heliox, 80% helium, and 20% oxygen added to a secondary oxygen gas source through the dry side of the humidifier chamber. The algorithm for setting HFNC gas flows was as follows: estimated tidal volume for a child $\times$ respiratory rate = estimated expiratory minute volume. Our goal was to set the total gas flow at 3.5 $\times$ expiratory minute volume. In our patient, the estimated tidal volume was 35 mL, and the respiratory rate was 70 breaths/min, so tidal volume $\times$ respiratory rate = 2.4 L. Then, 3.5 $\times$ 2.4 L gave us a target gas flow of at least 8 L/min. To implement this target, a heliox-calibrated CGA-280 regulator (Best Corporation, Lombard, Illinois) with flow meters connected to a G cylinder (4,000 L) was

brought to the bedside and attached via T connector to the 100% oxygen source for the HFNC.[9,11] The F_{IO_2} was verified via an oxygen analyzer as the gases entered the humidifier chamber. The conventional oxygen analyzer was not affected by the 80:20 heliox gas mixture.

Before heliox initiation, assessment showed a respiratory rate of 60–70 breaths/min with + 4 to + 5 suprasternal chest retractions and nasal flaring. The patient's arterial oxygen saturation (SpO_2) was 94% on HFNC at 5 L/min, and he intermittently desaturated to 84%. Heliox was started using an 80:20 specialty gas mixture at 8 L/min with 100% oxygen at 1 L/min to produce a final concentration of 70% helium, $F_{IO_2} = 0.30$, and a total gas flow of 9 L/min.

One minute after heliox initiation, the patient's respiratory rate fell to 31–36 breaths/min, and suprasternal chest retractions improved to subcostal chest retractions of + 2 to + 3 with improved nasal flaring. His breath sounds remained coarse, but he appeared to have improved and was resting more comfortably. The SpO_2 remained in the lower 90s. Heliox was then titrated to 60% helium and $F_{IO_2} = 0.40$. The primary heliox flow decreased to 7 L/min, and the secondary oxygen flow increased to 3 L/min. The total gas flow was set at 10 L/min, and SpO_2 improved to 96%. At one point during the first 24 h of treatment with heliox, the patient's respiratory rate increased to 60 breaths/min, SpO_2 fell to 89%, retractions worsened, and nasal flaring returned. Upon investigation, his heliox gas line had become disconnected from the HFNC circuit. Once the heliox was reconnected, the respiratory rate again decreased to 27 breaths/min, and SpO_2 improved to 96%. After heliox initiation, the patient's condition improved from critical to serious/stable.

Given the diagnosis of acute bronchiolitis, aerosolized Pulmicort (0.25 mg) was added to reduce airway inflammation. This treatment was given every 12 h with heliox-augmented HFNC. No respiratory deterioration was observed during treatments. With improvement in his respiratory status, handheld albuterol nebulizer treatments were decreased to every 4 h as needed, chest physical therapy remained at every 2 h, and Pulmicort was administered every 12 h. Nutritional support was implemented on day 1 of heliox administration.

The patient remained on 60/40 heliox via HFNC overnight. He received one racemic epinephrine treatment (2.25%) with heliox-augmented HFNC with no change in perceived work of breathing. The next morning, the patient appeared to be resting more comfortably, with no further episodes of SpO_2 desaturation. Later in the day, the patient's SpO_2 was 100% on 60% helium and $F_{IO_2} = 0.40$, so the oxygen concentration was decreased to 30% (70% helium). The patient's condition was upgraded to fair. On day 3, heliox was discontinued; on day 10, the patient was discharged from the pediatric ICU to a floor for continued treatment; and 7 d later, he was discharged home with clinic follow-up.

Discussion

Our patient was extubated and exhibited severe respiratory distress. Although subglottic or upper airway edema may have been present, acute bronchiolitis related to coronavirus infection was a likely cause of the severe acute respiratory distress. Regardless of the possible contributions, our patient appeared to respond immediately and significantly to inhaled oxygen-helium mixtures.

The use of heliox as medical therapy was first reported in 1935 by Alvin Barach,[1] who observed that breathing heliox appeared to relieve dyspnea in adults and children with asthma and upper airway obstruction. Although this and other early reports were non-controlled, the rapid improvement observed in patients strongly suggested an immediate effect of breathing heliox on R_{aw}. In addition, as witnessed in our case, relapse occurred when heliox was discontinued even briefly.[3] Few prospective studies have examined the use of heliox in acute viral bronchiolitis. Martinón-Torres et al[12] investigated 38 infants with respiratory syncytial virus-related respiratory infection using a modified version of Wood's clinical asthma score. They found significant improvement in scores with heliox after 1 h of treatment compared with the control group. The total average decrease in scoring was 4.2 in the heliox group versus 2.5 in the control group.[12] Kim et al[13] performed a randomized controlled trial with 69 infants with bronchiolitis and found a mean change from baseline of 1.84 in the modified Wood's clinical asthma scores for the heliox (70/30) group versus 0.31 for the oxygen group. However, neither study described heliox gas flows for mask or HFNC delivery systems. The only prospective study for the use of heliox in the treatment of acute bronchiolitis in spontaneously breathing children was performed by Hollman et al.[14] Subsequent controlled trials demonstrated a reduction in R_{aw} in severe acute status asthmaticus during heliox inhalation as well as improvement in efficacy of inhaled bronchodilators delivered during inhalation of heliox mixtures.[4]

The beneficial effects of breathing heliox mixtures likely derive from reduction in air-flow resistance and restitution of non-turbulent gas flow in the airways. In normal human airways, the resistive pressure decrease between the glottis and tenth-generation airway varies directly with the density of inspired gas, and gas flow is turbulent. The resistive pressure decrease over the tenth to twentieth generations is density-independent because air flow in these regions is laminar. Because 80% of the inspiratory resistive pressure decrease occurs in the more proximal density-dependent segments, breathing the less dense heliox can reduce R_{aw} to 28–49% of that measured with air in normal patients.

Because R_{aw} in normal patients is < 3 cm H_2O/L/s, this 40% pressure reduction is clinically unimportant. However, in asthma and other causes of air-flow obstruction (subglottic edema, acute bronchiolitis), R_{aw} can increase to 30–50 cm H_2O/L/s, with much of this increase related to turbulent gas flow.[3] In small children with acute air-flow obstruction from bronchiolitis, studies indicate that severe acute bronchiolitis is a heterogeneous disease and involves mainly the smaller lower airways but also lung interstitium.[12,13] Because heliox reduces non-laminar flow, diverse causes of airway disease leading to air-flow obstruction and turbulence are likely to respond to heliox use.

The use of heliox in airway disease with severe acute air-flow obstruction does not treat the underlying disease or influence the anatomy of the airway. Rather, heliox is used as a bridge treatment to reduce R_{aw} and reduce respiratory muscle work until definitive therapies and time act to reduce R_{aw} and eliminate the need for heliox breathing, usually within 24–48 h.[11]

To be effective in reducing R_{aw}, helium concentrations must be ideally above 70% of the inhaled gas mixture. Such high concentrations will limit the F_{IO_2} that can be administered simultaneously.[11] Schaeffer et al[10] demonstrated that hypoxemia associated with airway disease is modest and permits use of heliox with small amounts of supplemental oxygen added because the underlying mechanism of gas-exchange impairment is ventilation-perfusion mismatching during status asthmaticus.

We used the Aeroneb Solo system to deliver inhaled agents. The Aeroneb can be placed on the dry or wet side of the HFNC circuit. In this system, there is limited contact with the patient, which is ideal for patients who do not like being touched. The Aeroneb is a micropump nebulizer that uses a domed aperture plate with holes that control the size of the aerosol droplets and a vibrational element that aerosolizes the medication. Another approach is to deliver agents via a heliox-powered jet nebulizer. Hess et al[15] reported previously that heliox-powered jet nebulizers generate significantly smaller particles and a lower inhaled mass of albuterol.

To reduce patient agitation, we also used a nasal cannula instead of a mask to deliver the medication. Although this strategy results in significant (40–90%) loss of medication, the use of heliox improves the efficiency of aerosolized albuterol delivery via the Aeroneb device.[16] Ari et al[9] studied the combination of HFNC, Aeroneb, and heliox in vitro for the pediatric model and reported that as gas flow increased from 3 to 6 L/min with heliox, Aeroneb aerosol delivery increased by 2-fold compared with oxygen as the driving gas. Another in vitro study found between 18 and 26% dose delivery using a pediatric nasal cannula and concluded that aerosols can be efficiently delivered via HFNC.[17] On the basis of the results, we believe that although efficiency is low, delivery is stable, and sufficient medication can be delivered to exert a clinical effect.

To our knowledge, this is the first report of heliox being administered via HFNC for the treatment of acute bronchiolitis related to HCoV respiratory infection. We hypothesize that the combination of treatments may have had a cumulative therapeutic effect for attenuation of acute air-flow obstruction. Clinically, our patient's breathing improved immediately with heliox treatment, and his general condition continued to improve after 48 h of heliox, aerosolized corticosteroids, and nutritional support. The benefit of heliox itself appeared to be immediate and served as a bridge to support the patient while time and pharmacologic measures took effect and an underlying infection abated.[18-20] Because patient responses may vary, we believe that a trial of heliox should be considered when caregivers are confronted with patients with severe air-flow obstruction who still have respiratory reserve. The patient must be monitored closely throughout the administration of heliox for acute changes, and blood gas determination or transcutaneous P_{aCO_2} monitoring should ideally be performed. More prospective clinical studies are needed to further define the patient population that may respond to heliox, HFNC, and aerosolized corticosteroids for the treatment of severe acute bronchiolitis exacerbation, which is now documented to be caused by an increasing number of viral agents.[6,21-23]

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