The Use of Heliox in Children

a report by
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Helium (He) is an odorless, tasteless, inert gas with few medicinal or pharmacological properties when administered alone. As helium is biologically inert, there are no known toxic effects, even when administered for prolonged periods of time. The flow of air through a fixed obstruction or orifice is always at least partially turbulent, and inversely proportional to the square root of gas density. Helium's lower molecular weight and subsequent density (compared to other gases found in air) should promote laminar flow through an obstructed or fixed orifice without a gas viscosity difference.

In 1934, Dr Alvan Barach first described the medicinal use of helium for resolution and treatment of upper airway obstruction lesions.[1] Typically, helium is combined with oxygen (O_2) and referred to by the medical community as heliox. In a heliox gas mixture, helium replaces nitrogen and is generally delivered in concentrations that are three to four times higher than that of oxygen (i.e. 80:20 or 70:30). Since that first description by Barach, heliox gas mixtures have been used and promoted as adjunctive therapy to respiratory diseases and airway lesions for over 70 years. Despite the medical community's gravitation toward evidence-based medicine in the 21st century, the clinical effectiveness of heliox in pediatric patients with airflow obstruction is relatively sparse and is reported primarily through case presentations, case series, or small, uncontrolled studies. This article is designed to provide a brief evidence review for heliox treatment of children with asthma, airway obstruction, bronchiolitis, and croup.

Asthma

Asthma is a chronic inflammatory disease of the airways that has components of airway hyper-reactivity and airflow obstruction due to smooth airway muscle constriction. While helium has no bronchodilating or anti-inflammatory properties, its lower density and its ability to promote laminar airflow through obstructive airways has several theoretical benefits for patients with asthma. In two frequently cited trials, the use of heliox in pediatric asthma demonstrated different outcomes.[2,3] Kudukis et al. utilized 80:20 heliox in 18 children with asthma in the emergency department (ED) and documented significant improvement in pulsus paradoxus, dyspnea score and peak flow measurements in the heliox group.[2] Carter et al., in another trial administering 70:30 heliox to 11 children hospitalized with asthma exacerbations, demonstrated no differences in clinical or dyspnea score, forced expiratory volume in one second (FEV_1), and forced vital capacity (FVC).[3] There was a slight improvement in peak flow in the heliox group.

A more recent interest in heliox as a gas source for nebulization of asthma medications has been described in the literature. Kim et al. published the first prospective, randomized, single-blind pediatric study of heliox-driven albuterol nebulization with moderately to severely ill pediatric asthmatic patients. The investigators found that continuous heliox-driven nebulization of albuterol early in the course of ED care substantially improved the Pulmonary Index score and the unblinded discharge rate at the 12-hour treatment point. Rivera et al. studied a similar pediatric asthmatic population; however, this group reported no significant differences in Modified Dyspnea Index scores at 10 minutes or 20 minutes after the initiation of heliox-driven albuterol therapy. The ability to establish a convincing argument for the use of heliox for asthma from these four studies is largely inconclusive. Many questions regarding heliox treatment strategies and regimens for acute asthma remain unanswered, and there is a need for additional studies to clearly define any potential beneficial role of heliox for acute asthma exacerbations.

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1. *Barach A, "The use of helium in the treatment of asthma and obstructive lesions in the larynx and trachea",* Ann Intern Med *(1935);9: pp. 739–65.*
2. *Kudukis T M, Manthous C A, Schmidt G A, et al., "Inhaled helium-oxygen revisited: effect of inhaled helium – oxygen during the treatment of status asthmaticus in children",* J Pediatr *(1997);130: pp. 217–224.*
3. *Carter E R, Webb C R, Moffitt D R, "Evaluation of heliox in children hospitalized with acute severe asthma. A randomized crossover trial",* Chest *(1996);109: pp. 1,256–1,261.*

Upper Airway Obstruction

The etiology of upper airway obstruction can occur from a multitude of diseases or conditions. The resulting increase in airway resistance and the work of breathing in anatomically smaller airways is a recipe for respiratory failure in children. The ability of heliox to improve gas flow and oxygenation, as well as decrease the work of breathing, makes heliox an ideal approach for airflow obstruction lesions in the upper airways. Grosz and colleagues evaluated heliox effects on 42 children admitted and treated (44 occurrences) for significant upper airway obstruction.[6] Using largely anecdotal criteria for work of breathing, 32 (73%) of the children had a positive response to heliox—the exception was for children with a history of congenital anomalies or syndromes (67%). Connolly and McGuirt treated 14 consecutive patients with severe subglottic edema or injury and meeting intubation criteria with heliox.[7] All children without a prior history of subglottic stenosis (71%) were successfully and safely managed on heliox, and avoided intubation.

Rodeberg and colleagues evaluated heliox in eight children with post-extubation stridor from burns.[8] Helium concentrations (50–70%) demonstrated a decrease in respiratory distress and thus avoided reintubation. In this trial, heliox was able to successfully relieve stridor, reduce respiratory distress and prevent reintubation in children with burns and post-extubation stridor. Kemper and colleagues also evaluated heliox's success in reducing post-extubation stridor in 13 children with burns and trauma.[9] Respiratory distress scores for heliox were significantly improved. Kemper and colleagues concluded that heliox was successful in decreasing a stridor score for children with post-extubation stridor and was a preferred method of treatment. Although the evidence is largely from uncontrolled trials, heliox therapy for upper airway obstruction has demonstrated the ability to reduce stridor, reduce respiratory distress, and the work of breathing. Furthermore, heliox may lessen the need for post-extubation reintubation in children with upper airway obstructive disorders or diseases.

Continuous heliox-driven nebulization of albuterol early in the course of ED care substantially improved the Pulmonary Index score and the unblinded discharge rate at the 12-hour treatment point.

Croup (Laryngotracheobronchitis)

The most common etiology of croup syndromes is acute viral laryngotracheitis, which creates inflammation of the subglottic tissue and possibly tracheal mucosa inflammation, resulting in swelling and narrowing of the upper airway. Duncan et al. utilized heliox in the treatment of seven children with acute airway obstruction—two by croup and the others by mass effect or post-extubation edema.[10] Heliox treatment significantly decreased croup scores and improved gas exchange. Terregino et al. conducted a prospective, double-blind, controlled ED trial of 15 pediatric patients with mild croup, randomized to receive either 30% humidified oxygen or 70:30 humidified heliox.[11] Heliox resulted in a greater improve-ment in croup score (p=NS). Weber and

4. *Kim I K, Phrampus E, Venkataraman S, et al., "Helium/Oxygen-Driven Albuterol Nebulization in the Treatment of Children With Moderate to Severe Asthma Exacerbations: A Randomized, Controlled Trial",* Pediatrics *(2005);116(5): pp. 1,127–1,133.*
5. *Rivera M L, Kim T Y, Stewart G M, et al., "Albuterol nebulized in heliox in the initial ED treatment of pediatric asthma: a blinded, randomized controlled trial",* Am J Emer Med *(2006);24: pp. 38–42.*
6. *Grosz A H, Jacobs I N, Cho C, Schears G J, "Use of helium-oxygen mixtures to relieve upper airway obstruction in a pediatric population",* Laryngoscope *(2001);111(9): pp. 1,512–1,514.*
7. *Connolly K M and McGuirt W F Jr., "Avoiding intubation in the injured subglottis: the role of heliox therapy",* Ann Otol Rhinol Laryngol *(2001);110(8): pp. 713–717.*
8. *Rodeberg D A, Easter A J, Washam M A, et al., "Use of helium-oxygen mixtures in the treatment of postextubation stridor in pediatric patients with burns",* J Burn Care Rehabil *(1995);16(5): pp. 476–480.*
9. *Kemper K J, Ritz R H, Benson M S, et al., "Helium-oxygen mixture in the treatment of postextubation stridor in pediatric trauma patients",* Crit Care Med *(1991);19: pp. 356–359.*
10. *Duncan P G, "Efficacy of helium-oxygen mixtures in the management of severe viral and post-intubation croup",* Can Anaesth Soc J *(1979);26: pp. 206–212.*

colleagues evaluated the additive effect of 70:30 heliox with racemic epinephrine in 29 children with moderate to severe croup.[12] A reduction in croup score occurred with both heliox and racemic epinephrine, and the authors concluded that racemic epinephrine and heliox demonstrated equal treatment efficacy. Heliox administered to croup patients results in an improvement in croup scores and may result in a reduction in respiratory distress. However, these results may not be significantly different from other conventional therapies, except for heliox's extremely safe side-effect profile. In fact, combining heliox with conventional therapies may provide a better overall effect than either approach carried out separately.

positive-pressure ventilation, endotracheal intubation, or time to intubation) or secondary outcome (clinical scores, oxygen requirement, $PaCO_2$, duration of study gas administration, or Pediatric Intensive Care Unit (PICU) length of stay) measures.

Martinon-Torres et al. compared 70:30 heliox with nebulized epinephrine in 38 non-intubated infants with moderate to severe RSV bronchiolitis.[15] Clinical score, heart rate, respiratory rate, and oxygen saturation improved in both groups. Infants treated with heliox demonstrated a more rapid improvement in clinical score, respiratory rate, and heart rates at one-hour and at the end of the observation period. PICU length of stay for the heliox group was also significantly shorter than the control group. While evidence is limited, heliox appears to decrease the work of breathing and improve gas exchange for infants with bronchiolitis in non-intubated infants with moderate to severe respiratory distress.

The ability of heliox to improve gas flow and oxygenation, as well as decrease the work of breathing, makes heliox an ideal approach for airflow obstruction lesions in the upper airways.

Bronchiolitis

Bronchiolitis is an infectious disease caused primarily by the respiratory syncytial virus (RSV), parainfluenza virus and *Haemophilus* influenza virus. These viral infections result in inflammation of the respiratory bronchioles, producing airway obstruction from bronchiole wall edema and excessive mucus. Since bronchiolitis is associated with airways, conventional wisdom implies that heliox therapy may offer clinical benefits. Hollman and colleagues compared heliox with oxygen-enriched air in 18 infants with RSV bronchiolitis.[13] The Clinical Asthma Score decreased in all 18 patients and were most pronounced in infants with the most severe airflow obstruction.

Liet and colleagues evaluated heliox's ability to reduce the initiation of positive-pressure ventilation in 39 infants with severe bronchiolitis and respiratory failure.[14] The results showed that there was no difference between groups for the primary outcome (reduction of

Summary

The difficulties in delivering heliox to children with acute airflow obstruction may play a role in the largely controversial and anecdotal evidence that exists for treatment effectiveness. Logically, the relatively safe profile of heliox therapy, coupled with its rapid onset of action upon initiation, should enable clinicians to consider heliox as a 'therapeutic bridge'. This would allow heliox to reduce the work of breathing, improve distribution of ventilation, reduce minute volume requirement, and improve aerosol delivery, while allowing other strategies or treatment regimens to be initiated or take clinical effect on the underlying etiology of the airflow obstruction. ■

11. *Terregino C A, Nairn S J, Chansky M E, et al., "The effect of heliox on croup: A pilot study",* Acad Emerg Med *(1998);5: pp. 1,130–1,133.*
12. *Weber J E, Chudnofsky C R, Younger J G, et al., "A randomized comparison of helium-oxygen mixture (heliox) and racemic epinephrine for the treatment of moderate to severe croup",* Pediatrics *(2001);107: p. E96.*
13. *Hollman G, Shen G, Zeng L, et al., "Helium-oxygen improves Clinical Asthma Scores in children with acute bronchiolitis",* Crit Care Med *(1998);26: pp. 17,31–1,736.*
14. *Liet J M, Millotte B, Tucci M, et al., "Noninvasive Therapy with Helium-Oxygen for Severe Bronchiolitis",* J Pediatr *(2005);147: pp. 812–817.*
15. *Martinon-Torres F, Rodriguez-Nunez A, Martinon-Sanchez J M, "Heliox therapy in infants with acute bronchiolitis",* Pediatrics *(2002);109: pp. 68–73.*