Heliox therapy

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Introduction

The medical use of helium-oxygen mixture (heliox) was first described as a therapy for asthma and airway obstructions in 1934 by Barach[1]. Recently, heliox applications have expanded from airway obstruction[2] and asthma[3] to bronchiolitis[4-6] and chronic obstructive pulmonary disease[7,8] (COPD). Helium is an odorless, colorless, noncombustible, biologically inert gas, and has other physical properties that make it medically useful when mixed with oxygen (Table 1). The advantage of heliox is primarily derived from its lower density than either oxygen or air. Heliox may provide some advantages to air or oxygen alone in patients in respiratory distress (Table 2). The lower density reduces airway resistance and thus

Low Density
Converts Turbulent Flow to Laminar Flow
High Thermal Conductivity
Biologically Inert
Higher Carbon Dioxide Diffusion Rate

Table 1. Physical Properties of Heliox

Decrease work of breathing
Decrease airway pressure
Improve tidal volume
Improve CO_2 elimination
Improve distribution of ventilation
Improve oxygenation
Decrease dynamic hyperinflation and air trapping
Reduce inflammatory cell filtration
Reduce atelectasis

Table 2. Purported Respiratory Benefits of Heliox

reduces patient work of breathing and the driving pressure required to achieve adequate ventilation. The mechanism of improved ventilation efficiency may be by conversion of turbulent flow to laminar flow and improved gas mixing in distal airways. Heliox can also reduce air-trapping and dynamic hyperinflation; it can pass through obstructed airways more easily than air or oxygen, and has a higher carbon dioxide diffusion rate. Heliox ventilation may recruit additional gas exchange units and reduce overall required oxygen and ventilatory support. Heliox can be a technically challenging therapy for the clinician to administer, due to the relative scarcity of medical equipment designed specifically for heliox gas mixtures. The real risks of heliox therapy are few since heliox does not interact with any body tissues. The most significant hazard of heliox delivery is brain anoxia from the inadvertent administration of less than 21% oxygen. Due to tank availability and gas costs, some institutions utilize 100% helium tanks and bleed in oxygen to achieve the desired heliox concentration. With this set-up, if the oxygen source becomes disconnected, the patient can receive 100% helium and be deprived of oxygen. This practice poses a significant risk to the patient and can not be recommended. Heliox has a six times higher thermal conductivity than air. In order to avoid significant heat and moisture loss, especially in the pediatric patient, it is very important to adequately heat and humidify heliox whenever possible. The low density and high thermal conductivity of heliox can also interfere with the proper functioning of medical equipment. If you are unfamiliar with the properties of heliox, and its interactions with medical devices designed for air or oxygen, it is also possible to deliver dangerously high lung volumes that can be harmful to the patient.

Respiratory Disorders Treated with Heliox

Heliox has been utilized in a variety of respiratory disorders (Table 3) with varying degrees of frequency and success. The most common use for heliox is for upper airway obstruction. Conditions such as airway tumors, post-extubation stridor, tracheomalacia, subglottic stenosis, croup, and tracheitis, are all likely to respond to heliox administration. Children, who have smaller airways to begin with, are the most likely to receive the greatest benefit. Severe post-extubation stridor is often treated with the reintroduction of the artificial airway, further compounding the injury to the surrounding tissues, and prolonging the hospital course. Heliox therapy in these instances, can decrease the work of breathing, improve oxygenation

Upper Airway Disorders	Lower Airway Disorders
Croup	Asthma
Tracheitis	COPD
Post-Extubation Stridor	Cystic Fibrosis
Tumor or other Masses	Pneumonia
Foreign Body Aspiration	Bronchiolitis
Tracheomalacia	Bronchiectasis
Tracheal and Subglottic Stenosis	ARDS
Epiglotitis	Respiratory Distress Syndrome (RDS) Bronchopulmonary Dysplasia (BPD)

Table 3. Respiratory Disorders Treated with Heliox

and ventilation, and alleviate the need for artificial airways and mechanical ventilation, until curative therapy can be implemented. Grosz et al[2] retrospectively evaluated 42 children ages 1-14 years with upper airway obstruction. Overall, 73% (32) of the children demonstrated a decrease in work of breathing with heliox therapy. Often the most challenging aspect is correctly selecting patients who will benefit from heliox therapy. While all the children who were born prematurely were positive responders to heliox in this study group, 67% of the children with congenital anomalies were non-responders.

Heliox can also be effective in lower airway disorders such as asthma, bronchiolits, Neonatal Respiratory Distress Syndrome (RDS), and COPD. The hallmarks of asthma, airway inflammation and bronchoconstriction, make it likely that heliox therapy would be of benefit to these patients. The clinical studies of heliox therapy for asthma have mixed results, most likely due to design issues such as patient selection. Appropriate patient selection is important, as the majority of asthmatics will respond to standard asthma therapy alone. Heliox appears to be most effective in those with the greatest degree of airway obstruction and in the most severe distress. Early use of heliox can decrease work of breathing, subjective feeling of dyspnea, improve oxygenation and ventilation, and prevent intubation and mechanical ventilation. During mechanical ventilation of the asthmatic patient, heliox can be life saving, by dramatically improving gas exchange and decreasing dangerously high airway pressures. Bronchiolitis is one of the most common infectious diseases affecting infants, and one of the most promising newer applications for heliox. Airway edema, inflammation, and abundant mucous production can lead to severe airway obstruction and respiratory failure in these infants. Current therapy relies on supportive care, such as adequate hydration, supplemental oxygen, and nasal suctioning. Early reports by Brown[4,5] reported the combination use of heliox and nasal continuous positive airway pressure (nCPAP) to decrease respiratory distress and prevent mechanical ventilation in these infants, as well as heliox mechanical ventilation to dramatically decrease blood carbon dioxide levels, increase blood pH, and minimize airway pressures. Martino-Torres et al[6] subsequently combined heliox with nCPAP in 15 infants and documented an improvement in clinical score, $PaCO_2$, respiratory rate and oxygen saturation, with only one heliox treated infant requiring intubation and mechanical ventilation.

Unfortunately, there are few heliox clinical studies in the area of neonatal respiratory diseases. The physics of ventilating patients with extremely small airways would seem to lend itself to this therapy, and early studies of heliox therapy in the neonatal intensive care unit (NICU) were very promising. In 1993, Elleau et al[10] reported results of a randomized controlled trial of heliox versus standard gas mixtures in 27 mechanically ventilated premature infants with RDS (30 weeks, 1200 grams) who did not receive surfactant. The heliox infants had a significantly improved PaO_2/FiO_2 ratio by day two and required significantly less support by day four. A majority, 10/13, of the heliox infants were extubated by day eight, versus just 5/14 of the control group ($p<0.05$). Bronchopulmonary dysplasia (BPD) developed in only 2/13 of the heliox group, while 7/14 of the control group developed the disease. In today's NICU, preventing the introduction of invasive mechanical ventilation with its well recognized hazards is a cornerstone of care for the premature neonate. It is highly likely that the combination of heliox and nCPAP, already being studied and utilized today for bronchiolitic infants in the pediatric intensive care unit (PICU), would also be effective in the premature infant with RDS for preventing respiratory failure, BPD, and invasive mechanical support. Heliox in combination with high frequency ventilation and inhaled nitric oxide are also promising areas of future heliox research in the NICU.

Adult patients with COPD represent a large group that could potentially benefit from heliox therapy. Standard respiratory therapy for COPD includes oxygen, inhaled bronchodilators, and noninvasive positive pressure ventilation (NPPV). During severe exacerbations, patients may require intubation and mechanical ventilation. Patients with COPD requiring invasive mechanical ventilation are at high risk of complications of ventilation including pneumonia, prolonged ventilator dependence, need for tracheostomy and long intensive care unit (ICU) and hospital stays. Heliox therapy might increase expiratory flow in COPD patients and decrease dynamic hyperinflation, decrease work of breathing, improve oxygenation and ventilation, and prevent respiratory failure. If mechanical ventilation could be avoided, ICU and hospital stay might be decreased. One of the main questions under investigation is how to deliver heliox to COPD patients. Is it advantageous to deliver it through a face mask system, in conjunction with NPPV, or in addition to mechanical ventilation? Jolliet et al[7] studied whether heliox in conjunction with NPPV would decrease intubation rate, or decrease hospital costs. Intubation rate was 20% for the control group versus 13% for the heliox group with a shorter post ICU stay and overall hospital costs for the heliox group. Although not statistically significant in this small trial, these results may be clinically significant and larger studies should be attempted to clarify these results.

Heliox Delivery

Heliox therapy is of very little clinical value to patients who are in a mild disease state. Therefore, heliox therapy should only be offered to patients with a disease severity requiring either intensive care or at the very least requiring continuous cardiopulmonary monitoring. The patient's respiratory status and the heliox delivery equipment should be assessed by a skilled clinician at least every two hours. Before initiating heliox therapy, the clinical staff should have adequate training to safely and effectively deliver the gas and resources on hand such as hospital policies or procedures to guide their care. Since few institutions have heliox piped directly into the intensive care unit, most rely on cylinders of gas brought by hand to the bedside. In the United States, the most common concentrations available are "H" size 80% helium/20% oxygen (80/20) and 70% helium/30% oxygen (70/30). These tanks contain approximately 4,500 liters of gas, which will provide an average of approximately five hours of heliox therapy, depending on the delivery device selected. Tank costs range from approximately $65.00-$100.00 in the U.S. For patient and staff safety, large tanks should only be moved while confined in hand carts and should be secured at the bedside in an appropriate tank stand. Before initiating therapy, the clinician must verify the contents of the tank by reading the label and analyzing the oxygen content. Only medical grade heliox should be delivered to a patient. Clinicians should also assure a minimum of 24 hours of heliox gas is always readily available and that the tanks are not stored where they are exposed to extreme heat or cold. Special heliox regulators are required to deliver the gas to a patient and wrenches are necessary to attach them to the tank. Although helium and heliox flow meters are available commercially, many clinicians will utilize air or oxygen flow meters to deliver heliox, since they are already readily available. Heliox will flow through an opening faster than air or oxygen, so a correction factor must be utilized to accurately estimate flow, when utilizing an air or oxygen flow meter for heliox gas delivery. The factors are based on heliox concentration and generally rounded to 1.8 for 80/20, 1.6 for 70/30, and 1.4 for 60/40. For example, 10 liters per minute (L/min) of 80/20 heliox as measured while flowing through an air flow meter, is actually 18 L/min of 80/20 heliox. An oxygen analyzer, with active audible alarms, must be utilized in all heliox delivery configurations, to ensure oxygen delivery.

The oxygen alarm is also usually the first indication that there is a problem in the heliox delivery circuit. Although helium analyzers are available, an oxygen analyzer is usually readily available and can be used alone. As long as air is not allowed into the delivery system, the balance of the gas can be assumed to be helium. In order to titrate the amount of oxygen and helium being delivered to the patient, it is not uncommon for 100% oxygen to be bled into the heliox configuration. To function accurately, medical gas blenders incorporate a bleed flow. The wasting of heliox gas through the bleed flow makes medical gas blenders undesirable in most heliox configurations. Whenever feasible, to avoid excessive heat loss and secretion drying, all gases should be heated and humidified.

Although there are published cases of heliox therapy demonstrating a clinical effect with as little as 20% helium/ 80% oxygen (20/80)[10], heliox is the most effective at the highest concentrations. To achieve the greatest benefit for the patient, a completely closed system for heliox delivery should be utilized. When this is not possible, a system that is tight fitting, entrains very little or no room air, and fulfills the patients minute volume demands is necessary for clinical success. The non-rebreather valved resevoir oxygen mask is frequently used for heliox delivery. To be effective, all the one-way valves must be in place, especially the one between the mask and the reservoir bag. To adjust the heliox concentration, 100% oxygen flow is bled in using a T-connector, joining the flow from an 80/20 heliox tank and then measured with an oxygen analyzer. The combined flow is connected to the mask inlet and allows precision of the heliox concentration delivered to the patient. This is superior to the imprecise method of utilizing the 80/20 heliox tank as the only source for the mask and adding a nasal cannula to the patient for additional oxygen delivery. Although the non-rebreather oxygen mask may be the best option available to the clinician, it has limitations: It can be very difficult to get a tight fit and a lot of gas leakage can occur, or it may not provide enough flow to meet the patient's demands, entraining room air and decreasing the effectiveness of the gas delivery. Oxygen tents, hoods, and huts, would appear to provide a closed system alternative, however, they do not provide a viable option for heliox administration. The gas can separate and layer out within the enclosure with the potential for oxygen concentrations of less than 21% being delivered at the patient's nose and mouth.[11] Due to the high thermal conductivity of helium, there is also the high probability of hypothermia for the patient placed in a heliox tent, hood, or hut. Although there are reports of clinical success utilizing a nasal cannula for heliox delivery in children[12], this is also not an optimal delivery device. There are two primary problems with delivering heliox through a nasal cannula: The inability to meet the patient's minute volume demands, diminishing the effectiveness of the therapy, and the potential danger of delivering unmeasured, unmonitored, inadvertent positive airway pressure. Heated humidification systems designed to work with nasal cannulae are also necessary to minimize the loss of moisture and heat. A nCPAP device is superior to a nasal cannula to deliver heliox therapy, by providing a closed gas delivery system, built in alarms, active humidification, and the ability to deliver and monitor positive pressure. In a bench study Chowdhury et al[13] documented a 70-80% decrease in the work of breathing and a 30% increase in tidal volumes with heliox nCPAP compared to nitrox. The authors concluded that a nCPAP of 4cmH_2O is optimum for work of breathing and tidal volume when utilizing heliox with nCPAP.

Heliox and Aerosol Delivery

In most patients who are good candidates for heliox therapy there is also a clinical need to deliver inhaled medications, such as albuterol or racemic epinephrine. Several studies have shown that heliox can increase the amount of medication delivered to the lungs and could lead to greater bronchodilation of obstructed airways.[14-17] For the clinician, this can be the most technically challenging aspect of heliox therapy. Clinical success and the ability to adequately deliver medications will largely rest on the method used to deliver the drug. Generally, bronchodilators are nebulized with either an oxygen or air gas source by either a small or large volume nebulizer, and most nebulizers are not designed to be powered with heliox. Although studies show it can be very advantageous to have heliox present in the configuration, it is not necessary to power the nebulizer itself with heliox. In fact, most researchers advocate driving the nebulizer with oxygen, and adding heliox as a carrier gas to improve drug deposition. Utilizing heliox to power a nebulizer, can significantly decrease the size of the particles and the inhaled mass of the medication.[18] If the clinician utilizes heliox as a driving gas, flow to the nebulizer must be increased, in order to mimic the output of an oxygen driven system.[18] In addition, small volume nebulizers often do not meet the high inspiratory flow demands of patients in severe respiratory distress, causing room air dilution of the heliox and limiting aerosol medication delivery.[17] Studies demonstrate a more positive response for heliox, when a gas reservoir, or a large volume nebulizer, which functions like a gas reservoir, are utilized.[17] The Hope™ large volume heliox nebulizer (B&B Medical Technologies, Loomis, California) is specifically designed to be powered with oxygen, to allow the addition of heliox as a carrier gas, and it can meet the minute ventilation demands of the patient. (Figure 1) In patients who are on heliox mechanical ventilation, the simplest method for inhaled drug delivery is the metered dose inhaler (MDI). Garner et al[14] demonstrated that albuterol delivered to the end of the endotracheal tube (ETT) more than doubled, with heliox gas in the configuration, when administered by MDI, in a pediatric model of mechanical ventilation. Another good option for the delivery of inhaled medications, while

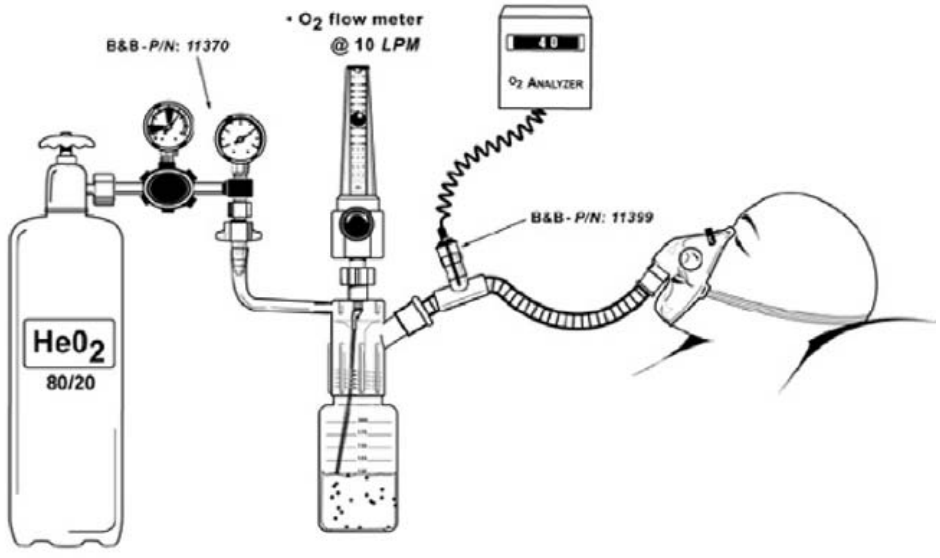

Figure 1 Hope™ Nebulizer (B&B Medical Technologies, Loomis, California) for Continuous Medication Delivery with Heliox

mechanically ventilated with heliox, is a nebulizer that does not require a gas flow to operate and does not add any additional flow into the circuit, such as the Aeroneb® Professional Nebulizer System (Aerogen, Galway, Ireland).

Heliox and Non-Invasive Positive Pressure Ventilation (NPPV)

NPPV is usually administered by ventilators designed specifically for this application. There is some evidence that the combination of NPPV with heliox can decrease work of breathing, alleviate dynamic hyperinflation, and prevent intubation and invasive mechanical ventilation.[8, 9] Some of the advantages of utilizing NPPV in conjunction with heliox, versus heliox through a non-rebreather mask are: the addition of positive end expiratory pressure (PEEP), active humidification, pressure supported breaths, and advanced monitoring. Unfortunately, laboratory testing has demonstrated a strong possibility of malfunction, when traditional NPPV ventilators are utilized for heliox administration.[19] Until recently, the safest option for the clinician, who would like to administer heliox and NPPV, is to utilize a suitable critical care ventilator in combination with a full face mask, instead of an ETT. A commercial heliox-delivery system could greatly simplify and improve heliox delivery for the clinician. The Aptaér heliox delivery system, (GE Healthcare, Madison, Wisconsin) which was released in the U.S. in 2004, did not provide essential features as FiO_2 control, PEEP or adequate

Figure 2 Inspiration™ LS Ventilator (eVent Medical, Galway, Ireland)

pressure support. The ability to add and adjust PEEP may be very important to compensate auto-PEEP in patients with obstructive disorders such as COPD and asthma.[8] The Helontix Vent™ (Linde Gas Therapeutics, Lindingo, Sweden) is awaiting approval in the United States and Europe. The Helontix Vent™ provides a unique combination of controls that has not been available previously in a NPPV/heliox format (Figure 2). In addition to control of pressure support from 3-30 cmH_2O, peak flow of 150 L/m, rise time 50-500 ms, and end flow detection 5-75%, PEEP from 0-10 cmH_2O can also be applied, and FiO_2 control from 21-100%. In addition the ability to adjust a constant flow of 5-60 L/min enables the ventilator to be used to treat a broad variety of patients.

Heliox and Mechanical Ventilation

In a 2005 survey[20] of the twenty-one area hospitals in San Diego, California, most hospitals (76%) reported utilizing heliox therapy, primarily in the intensive care units and the emergency department. Of those hospitals, just 29% reported using heliox in conjunction with mechanical ventilation, and most were likely to use the Galileo ventilator (Hamilton Medical, Rhäzüns, Switzerland) for this purpose. To be able to deliver heliox in conjunction with mechanical ventilation requires technical expertise, as well as a ventilator that will function safely and adequately with heliox. The low density and high thermal conductivity of heliox can affect the delivery and flow measuring devices of a ventilator that are designed to operate with air or oxygen. Often, tidal volume monitoring will underestimate the actual volumes delivered to the patient with heliox administration or the ventilator will cycle erratically. Gas mixing and oxygen analyzers can also be adversely affected by alternative gas administration. Some ventilators have oxygen or low minute volume alarms, which are activated with the addition of heliox. Frequently, the alarms can not be silenced; precluding their use as heliox delivery devices in some or even all situations.[21,22] The Puritan Bennett 840 ventilator (Pleasanton, California) will measure the density of the gases connected, and will not allow the delivery of heliox through the ventilator. In recent years, other manufacturers have begun to incorporate modifications for heliox delivery into their ventilators. The number and types of ventilators approved for use with heliox varies from country to country. In the U.S., only the AVEA ventilator (Viasys Healthcare, Yorba Linda, California) has completed the process and been approved by the United States Food and Drug Administration (FDA) for heliox delivery. Some devices like the Inspiration™ LS ventilator (eVent Medical, Galway, Ireland) (figure 3) have heliox

Figure 3 Helontix Vent™ Linde Gas Therapeutics, Lindingo, Sweden

features available in Europe that are awaiting FDA approval in the U.S. However, the Inspiration™ ventilator has been tested extensively with heliox, and is one of only a few that does function exceptionally well.[21] A large number of mechanical ventilators in use around the world have been laboratory tested with heliox mixtures and the results published to enable clinicians to make an educated and safe choice of a delivery device.[21-24]

Heliox mechanical ventilation can be started by first connecting the compressed air high pressure hose directly to a 50-psi 80/20 heliox tank. Most ventilators will function better when utilizing a heliox blend with an oxygen concentration close to 21%. A 100% helium cylinder should never be used due to the risk of asphyxia. Two heliox cylinders can be at the bedside in a "bank" system, connected together, so that an empty tank can simply be shut off and the full tank turned on without any interruption of gas delivery to a critically ill patient. The empty tank can then be replaced with another full tank at the clinician's discretion. A heated wire circuit humidifier should most likely be utilized during heliox mechanical ventilation due to the high thermal conductivity of helium, though no studies have compared this form of humidification with high-efficiency heat-moisture exchangers in the presence of heliox. Plastic sleeves that wrap around the circuit may be needed to maintain the temperature of the gas within the circuit and to prevent audible alarms condition from the humidifier. Any ventilator flow measuring device that utilizes the amount of heat loss to calculate flow will malfunction during heliox ventilation. Generally, this type of flow sensor must be removed during heliox ventilation, and other methods must be utilized to monitor the patient's condition. The disabling of a hot-wire flow sensor will typically prevent the use of volume targeted ventilation, features such as leak compensation usually must be disabled, and some of the patient monitoring capabilities will be lost without the sensor in place. Since heliox has no effect on pressure measurement or delivery, often the ventilator can be safely used in a pressure ventilation mode only. A ventilator that does not use a hot wire flow sensor and does not require any disabling of modes or features is greatly preferred for heliox delivery. Guidance for the medical management of heliox-driven mechanical ventilation in infants and children has been recently published by clinicians practiced in applying this therapy.[25] Recommendations for choosing appropriate ventilator settings as well weaning techniques are outlined in detail. Clinicians contemplating utilizing heliox in ventilated patients for the first time are advised to refer to the literature with respect to the ventilator in use in their institution, to develop a detailed plan including all necessary equipment, and to also seek input where appropriate from clinicians experienced in heliox use.

Key Major recommendations

The medical literature is rapidly expanding with some very promising studies underway in Europe and elsewhere around the world. In addition to upper airway obstruction and asthma; patients with RDS, bronchiolits, and COPD all have the potential to greatly benefit from heliox therapy. The introduction of many new products, manufactured specifically for use with heliox, should make heliox therapy safer and easier to apply. Clinicians must be aware of the unique properties of heliox, such as low density and high thermal conductivity, which make heliox difficult to interface with traditional respiratory care equipment. Mechanical ventilators designed for oxygen and air may deliver larger than expected tidal volumes and inaccurate oxygen percentages. Medication nebulizers function differently and drug deposition can be negatively effected, when powered with heliox rather than oxygen.

Aerosolized drug deposition to the lung can be increased by the addition of heliox to the circuit. Clinicians should choose either a device approved for heliox use or those that have been tested and published on extensively. Published ventilator tidal volume correction factors are readily available and should be used to enhance patient safety.

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