Special review

A Review of the use of Heliox in the Critically Ill

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ABSTRACT

Heliox, a mix of oxygen and helium, has a number of potential medical applications resulting from its relatively lower density. This paper reviews the physics underlying its utility and considers the evidence for its use. While there are studies that support its role, particularly in patients with exacerbations of asthma and chronic obstructive pulmonary disease (COPD), the data are inconclusive. (**Critical Care and Resuscitation 2006; 8: 64-72**)

Key words: Heliox, helium, airway obstruction, asthma, chronic obstructive pulmonary disease

Helium was discovered in 1868 by the French astronomer Pierre-Jules-Cesar Janssen during a spectroscopic study of a total solar eclipse in India. It was named later the same year by the British astronomer Joseph Norman Lockyer and chemist Sir Edward Frankland, the name derived from helios, the Greek for sun. It is an inert gas present in the atmosphere (0.00052%) and was used initially in airships and balloons.

Today, most commercial helium is recovered from natural gas using a cryogenic separation process, following which it is refined and liquefied. Liquid helium is shipped from the production site to various storage facilities worldwide before being distributed in the gaseous form into cylinders for on-site use.

Interest in the use of helium for medical purposes comes from the fact that helium is markedly less dense than both oxygen and nitrogen (see Table 1).[1] This confers the advantage of maintaining laminar gas flow in situations where turbulent flow might otherwise occur. For a given pressure difference, laminar gas flow will provide a greater flow-rate compared to turbulent gas flow. In conditions where a turbulent pattern of gas-flow exists, helium can increase the rate of gas-flow for a given pressure difference. Clinically this can be utilised to assist patients who suffer from airway narrowing.

Table 1. Physical properties of pure gases at RTP (298 degrees Kelvin and 1 atmosphere pressure)

	Density (ρ) Kg/m^3	*Viscosity (η) microPoise*	*Thermal conductivity W/m K*
Air	1.184	184.33	0.025
Carbon Dioxide	1.811	148.71	0.017
Helium	0.166	197.61	0.14
Nitrogen	1.167	177.82	0.026
Oxygen	1.33	205.35	0.026

RTP = room temperature and pressure

Helium mixed with oxygen, now known as heliox, has been used with upper airway obstruction and in exacerbations of asthma and chronic obstructive pulm-

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onary disease. However its use has been limited by a lack of strong evidence for its efficacy, availability and cost of helium gas mixtures, as well as impairment of normal ventilator functions. There is also the necessity to maintain a $FiO_2 < 0.4$ while using heliox in order to achieve a sufficient reduction in density essential for it to be beneficial. This reduces its utility in patients with a higher oxygen requirement.

Helium is biologically inert, insoluble and is eliminated within a few breaths. It is known to conduct heat approximately six times better than nitrogen, and thus its use can result in a decrease in body temperature. Inhaling heliox also causes an alteration in vocal pitch and may reduce the efficiency of coughing.

In Australia, helium is available in size C, D, E and G cylinders (410, 1400, 3500 and 7300L nominal capacity respectively) with the G size cylinder costing approximately $300 (2004 data; BOC Limited, North Ryde, Australia). In addition mixtures with oxygen are available in any combination the user requires. Mixtures with oxygen are colour coded brown with white shoulders while pure helium cylinders are brown alone. Heliox28 is a recently released dedicated delivery system with a fixed concentration of 28% O_2 and 72% helium. A 3500L cylinder of Heliox28 with integrated regulator and flowmeter costs $460 (2004 data; BOC Limited, North Ryde, Australia). This compares with $46 for an equivalent size cylinder of oxygen.

THE PHYSICS OF REDUCED GAS DENSITY

The effect on the nature of gas flow (laminar or turbulent) can be predicted by the effect of the decreased density of helium on the Reynolds number (Re). The Reynolds number is a dimensionless number that can be used to predict conditions of laminar or turbulent flow depending on the situation.

$$Re = \frac{\rho d \upsilon}{\eta}$$

where,

- υ = linear velocity (m/s)
- ρ = density of the gas (kg/L)
- d = diameter of the tube (m)
- η = gas viscosity (kg/m/s) (1 kg/m/s = 10 Poise)

Re > 4000 predicts turbulent flow and < 2000 laminar flow, where the flow of fluid is through a tube, such as gas transfer through airways.

In conditions where there is airway narrowing, heliox minimises the increase in the Reynolds number, increasing the likelihood of laminar flow being maintained. The importance of this lies in the relationship of flow to pressure.

During laminar flow, flow is described by Poiseuille's equation,

$$Q = \frac{\pi P r^4}{8 l \eta}$$

where,

- P = pressure
- Q = flow
- r = radius of the tube
- l = length of the tube

During turbulent flow,[2]

$$Q = [(P/k\rho)]^{0.5}$$

where k = a constant

Thus in laminar conditions flow is proportional to the pressure exerted, whilst in turbulent flow it is proportional to the square root of pressure. Hence changing from turbulent to laminar flow will result in a greater flow for a given driving pressure gradient.

Furthermore, in persistently turbulent conditions, the lower the density of the gas mixture the higher the flow for a given driving pressure. This is in distinction to laminar flow which is independent of density.

The flow of gases through narrow apertures is also subject to Graham's law of diffusion and Bernouilli's principle. The former ($R = [(1/\rho)]^{0.5}$ where R = Rate of diffusion) again implies that gases with lower densities (such as helium) have higher rates of flow for a given pressure. The latter (which states that as the velocity of a gas increases, the pressure it exerts decreases) suggests that the increased flow seen with heliox might result in a worsening of airway obstruction as there is less outward pressure exerted to help maintain airway opening. In practical terms, the benefits derived from maintaining laminar flow, together with a higher rate of flow due to Graham's law, is balanced with the potentially detrimental effects of Bernoulli's principle. This balance will determine the overall beneficial or detrimental effect of an alteration of gas density in conditions involving airway narrowing.

MEDICAL APPLICATIONS OF HELIUM

We searched the electronic databases (MEDLINE, EMBASE, and The Cochrane Library) for relevant articles using the search terms "heliox", "helium, "airway obstruction", "asthma", and "COPD".

The medical applications of heliox can be roughly divided into respiratory and non-respiratory, with the former being subdivided into upper and lower respiratory tract (Table 2).

Table 2. Medical applications of helium

Upper airway	*Lower airway*
Infection	asthma, COPD
croup	cystic fibrosis,
epiglottitis	bronchiectasis
laryngitis	bronchiolitis
tracheitis	lung cancer
Trauma and mass effects	HFOV
foreign body aspiration	
post extubation stridor[3,4]	
tumour	
Other	
tracheomalacia	
tracheal stenosis	
Other	
Assessment FRC	
IABP	
Operation and cooling of MRI scanners	
Treatment for	
Decompression sickness	
Pneumatosis cystoides[5]	
Hyperammonaemia[6]	

COPD = chronic obstructive pulmonary disease, HFOV = high frequency oscillatory ventilation, FRC = functional residual capacity, IABP = intra-aortic balloon pump, MRI = magnetic resonance imaging

Upper respiratory tract obstruction

The earliest reported use of helium-air mixtures for laryngeal and tracheal obstructive lesions dates back to 1935.[7] More recently there have been a number of case studies of patients, particularly children, treated with facemask heliox in an attempt to avoid intubation. Grosz et al looked retrospectively at 42 children who received helium-oxygen mixtures for upper airway obstruction within a three year period, of whom 32 (73%) had a subjective decrease in work of breathing.[8]

Connolly *et al*,[9] detailed 14 paediatric patients (five with viral tracheobronchitis, five with inflammatory exacerbations of subglottic stenosis, and four with acute iatrogenic subglottic injury) in whom heliox was used, avoiding intubation in ten. Heliox has also been used effectively in cases of bilateral vocal cord paralysis, for example post radiation therapy,[10] in post extubation stridor,[11] and as a temporising measure in cases of external tracheal compression due to tumour.[12]

Heliox has been used in a number of children suffering severe croup. Weber *et al*, measured croup scores in 29 children treated either with heliox via a non-rebreather mask or nebulised racemic adrenaline, and found similar improvements with both.[13]

Lower respiratory tract obstruction

1. *Heliox in Asthma*

Much of the recently published work on the use of heliox has been with refractory asthma. Heliox use aims to attenuate the increased work of breathing and respiratory muscle fatigue that is the hallmark of severe asthma. It is an attractive proposition but its role remains uncertain. Initial anecdotal reports suggested efficacy.[14-16] A number of trials have since been conducted concentrating on patients admitted to the emergency department with moderate - severe asthma or on intubated and mechanically ventilated patients. These represent two fundamentally different groups; in the first, heliox being used as an alternate first line therapy. In the second, it is used as therapy for intubated patients in whom first line measures have failed. In addition, there are a wide variety of end-points and heliox concentrations.

In non-intubated patients, there is a further division of studies into those using heliox to drive nebulisers containing beta-agonists[17-21] and those using heliox purely as an inhaled gas.[22-25]

In the former there are mixed results. The largest trial (n = 205) considered patients admitted to the emergency department with mild-moderate exacerbations of asthma. All received nebulised albuterol, with heliox (70:30) as the driving gas in 102 patients and oxygen in the remainder. End-points were peak expiratory flow rate (PEFR), FEV_1 and admission rates. There was no significant difference between the two groups.[20]

Similarly, Kress *et al*,[18] and Dorfman *et al*,[21] conducted prospective randomised controlled trials involving the use of heliox driven nebulised albuterol in deteriorating asthmatics admitted to the emergency department. Kress *et al*, found no difference in FEV_1.[18] Dorfman *et al*, noted no difference in PEFR and 5 patients in the heliox driven nebuliser group (n = 21) were hospitalised.[21] None of the control group (n = 19) required admission.

On the other hand, two studies have suggested some benefit with heliox in this context. Rose *et al*,[17] found a significant improvement in Borg dyspnoea score (a subjective measure of perceived dyspnoea scored 0 - 10) in 36 asthmatics (of whom 18 had heliox driven nebulisers) presenting to the emergency department. There was no difference in respiratory rate, FEV_1 or PEFR.[17] Bag *et al*, noted a significant improvement in FEV_1 with heliox driven nebulised albuterol in 31 stable asthmatics.[19]

Hess *et al*, demonstrated in a bench-test that using heliox as the nebuliser driving gas results in a smaller particle size.[26] This is due to the lower mass of heliox (as compared to nitrogen or oxygen) resulting in a

greater velocity change as the gas passes through the jet orifice of the nebuliser. This increases the velocity with which the solution impacts the baffle and results in a smaller particle size. This theoretically may confer a benefit with further deposition of bronchodilator in the distal airways. On the other hand, it also results in a lower mass of drug being delivered in a given period of time for a given flow. The possible implication of this is that using heliox at the same flow rates as air (as with the above studies) will not result in equal doses of drug being delivered.

In the case of heliox use as an inhaled gas in moderate - severe asthma, three groups have produced randomised trials involving a total of 52 patients. Two of these were based in the emergency department (one with adults,[22] the other with children[24]) and the third with paediatric inpatients. The latter (a randomised double blind crossover study) found a small but significant improvement in PEFR (56 ± 20% of expected versus 50 ± 16%, $p < 0.04$) and in FEF_{25-75} in favour of heliox compared to air in 11 patients.[23] There was no significant difference in FEV_1 or modified Borg dyspnoea score. The other study to involve children with status asthmaticus by Kudukis *et al*, observed a decrease in pulsus paradoxus during heliox breathing (from 23.3 ± 6.7 mmHg to 10.6 ± 2.8 mmHg, $p < 0.001$, $n = 10$), as well as a decrease in a non validated dyspnoea score. No difference was seen in control (air breathing, $n = 8$) patients.[24]

Kass *et al*, administered heliox (70:30) for 8 hours via a non-rebreather mask to 11 of 23 adults presenting to an emergency department. The remainder received air/oxygen at a FiO_2 of 0.3. There was a significantly greater improvement in PEFR in the heliox group (58.4% versus 10.1%) over the first 6 hours, but after 8 hours there was no significant difference.[22]

A recent Cochrane review on the use of heliox for non-intubated asthmatic patients,[27] as well as two other systematic reviews,[28,29] concluded that there was no evidence to support the use of heliox in this situation. Of note, no trials have been conducted that consider intubation rates, length of stay and mortality in asthmatic patients, hence there is insufficient data to comment on the beneficial or detrimental effects of heliox in influencing these clinically relevant end points.

As for intubated asthmatics, there have been only a very limited number of studies looking at the use of heliox in these patients. Shaeffer *et al*,[30] in a retrospective case control study, considered the change in A-a gradient over the first two hours of ventilation in 22 asthmatics ventilated either with heliox 80:20 ($n = 11$) or air ($n = 11$). They found a significant decrease in the A-a gradient in the group treated with heliox, and no change in the control group. Gluck *et al*,[31] reported a case series of seven ventilated patients with status asthmaticus treated with heliox (60:40) with resultant reduction in airway pressure, CO_2 retention and resolution of acidosis. To date there have been no randomised control trials in intubated patients. Furthermore, there is no study on the use of heliox with non-invasive ventilation in asthma, despite the fact that this form of ventilation is increasingly being used in decompensating asthmatics.

2. *Heliox in chronic obstructive pulmonary disease*

Heliox is theoretically beneficial in chronic obstructive pulmonary disease (COPD) exacerbations as it decreases airways resistance, resulting in a reduction of dynamic hyperinflation (intrinsic PEEP) which in turn reduces the work of breathing and should place the diaphragm and intercostal muscles in positions of greater mechanical advantage.

Again, the studies differ in terms of method of heliox administration and patient selection.

Only one study has considered the use of heliox driven nebulisers in exacerbations of COPD. de Biosblanc *et al*,[32] studied a group of 50 patients, 25 of whom received nebulised albuterol via a heliox (80:20) driven nebuliser. In the remainder, air was used as the driving gas. No difference was noted between the groups in the increase in FEV_1, while a significant improvement in FEF_{25-75} was seen in the heliox group.

Three studies involved the administration of heliox as an alternative to air via facemasks. Two of these (Swidwa *et al*[33] and Pecchiari *et al*[34]) involved patients with stable COPD. Swidwa *et al*, noted a decrease in $PaCO_2$ in 11 of 15 patients who received heliox for 15 minutes. Pecchiari *et al*, in a single blinded crossover study of 22 patients breathing air followed by heliox (or vice-versa) did not observe any difference in expiratory flow limitation (as assessed by the negative expiratory pressure method). Gerbeaux *et al*,[35] conducted a retrospective analysis of 81 patients who presented to the emergency department with exacerbations of COPD. All received standard treatment (terbutaline, ipratropium and prednisolone). Thirty nine were given heliox via a non-rebreather mask at 10 L/min, with the rest (42 patients) receiving air/oxygen. There was no blinding and it is unclear why the 39 patients were chosen to receive heliox (although both groups appear well matched). This group of patients had a significantly lower intubation rate (50% versus 8%, $p < 0.01$), mortality rate (24% versus 3%, $p < 0.01$) and length of ICU and hospital stay.[35]

Non-invasive ventilation is increasingly being used in the management of COPD exacerbations. We were able to identify four published studies combining the

use of heliox with non-invasive ventilation. The largest, a multicentre study published as yet only as an abstract, found a trend to lower intubation rates (20.8 vs 30.3%, $p = 0.13$) and mortality (8 vs 15%, $p = 0.14$) in 204 patients with a diagnosis of exacerbation of COPD and randomised to non-invasive ventilation with heliox ($n = 96$) or air/oxygen ($n = 99$).[36] A prospective randomised single blinded study considered 123 patients admitted to the intensive care unit of the three tertiary referral hospitals with the same diagnosis.[37] The control group ($n = 64$) were non-invasively ventilated initially with a mixture of air/oxygen with a PEEP of 5 cmH_2O and pressure support of 15 cmH_2O. The heliox group was given identical treatment with the substitution of heliox (78:22) for air/oxygen. There was a non-significant decrease in the intubation rate in the heliox group (13.5% versus 20.3%) and a shorter post-ICU length of stay in the non-intubated heliox patients. There was no difference in the mortality rate.

The two other trials are both crossover studies. Jolliet *et al*,[38] non-invasively ventilated 19 patients admitted with exacerbations of COPD with either heliox or air/oxygen for a period of 45 minutes followed by 45 minutes without ventilatory support and then by crossover. Peak inspiratory flow increased significantly when patients were ventilated with heliox (110 ± 20 L/min versus 78 ± 12 L/min, $p < 0.05$) and there was a significant decrease in inspiratory time. There was also a significantly greater decrease in Borg dyspnoea score (4.6 ± 1.6 to 2.8 ± 1.6 versus 4.5 ± 1.4 versus 3.7 ± 1.6, $p < 0.05$). Jaber *et al*,[39] studied ten ICU patients with "definite or highly probable" COPD either at admission to ICU ($n = 7$) or following the development of post extubation respiratory distress ($n = 3$). He found significant decreases in $PaCO_2$, pressure time index and work of breathing expended per unit time at high and low levels of pressure support using heliox as the inhaled gas (WOB per unit time at low level pressure support ventilation 7.8 ± 4.1 versus 10.9 ± 6.1 J/min, $p < 0.05$, and 5.7 ± 3.3 versus 9.2 ± 5.4 J/min, $p < 0.05$ at the higher level).

Finally, there have been studies involving patients intubated for exacerbations of COPD. Tassaux *et al*,[40] ventilated 23 patients with heliox for 45 minutes, followed by return to an air/oxygen mix. During the heliox ventilation in volume control mode there was a significant decrease in peak (30 ± 5 cmH_2O versus 25 ± 6 cmH_2O, $p < 0.05$) and mean airway pressures (8 ± 2 cmH_2O versus 7 ± 2 cmH_2O), intrinsic PEEP (9 ± 2 cmH_2O versus 5 ± 2.7 cmH_2O, $p < 0.05$) and trapped lung volume (215 ± 125 mL versus 99 ± 15 mL, $p < 0.05$).

Diehl *et al*,[41] investigated the effect of using heliox in patients with exacerbations of COPD just before and after extubation. He conducted a crossover study of 13 patients during which patients received heliox and air/oxygen for 20 minutes prior to and after extubation. Only five patients actually remained in the trial following extubation due to the inability of the remaining eight to breathe via a mouthpiece with a nose-clip. There was a significant decrease in work of breathing (1.133 J/L versus 1.442 J/L, $p < 0.05$) and intrinsic PEEP (2.1 ± 1.8 cmH_2O versus 2.9 ± 2.1 cmH_20, $p < 0.05$) using heliox prior to extubation. The results post extubation ($n = 5$) are non-significant.

Rodrigo *et al*,[42] produced a systematic review on behalf of the Cochrane group of the use of heliox in exacerbations of COPD. After methodological considerations, the review considered only 2 trials; the first that undertaken by Jolliet *et al* (see above),[37] and the second by de Boisblanc *et al*,[32] using heliox as the driving gas for a nebuliser containing beta-agonists. The Cochrane review did not support the use of heliox in COPD, quoting lack of evidence as the reason, a conclusion that is difficult to avoid.

3. *Heliox use in other conditions involving lower airway obstruction*.

Heliox has been used in a number of other clinical situations in which lower airway obstruction plays a significant role, particularly in children with bronchiolitis and cystic fibrosis. Heliox use in bronchiolitis has been found to have a benefit in two studies,[43,44] and no effect in another.[45] Again, the common theme is that heliox is a temporising measure but is not a treatment in itself.

4. *Other uses*

A recent study found that heliox improved exercise capability and Borg dyspnoea scores in lung cancer patients even in the absence of airway obstruction. The authors suggest in the discussion that this is due to a decrease in work of breathing and fatigue of respiratory muscles.[46]

Jaber *et al*,[3] have reported the use of heliox in patients with no background of obstructive lung disease in the post extubation period. In an unblinded crossover study conducted in a medical ICU, 18 patients received heliox or air in random order after extubation. Heliox led to a significant reduction in Pdi (transdiaphragmatic pressure, a measure of effort required to breathe) from 10.2 ± 0.7 cmH_2O to 8.6 ± 1.1 cmH_2O, $p < 0.05$ and improvement in patient comfort.[43] Symptoms of vocal cord dysfunction (usually inspiratory or biphasic wheezing) may also be dramatically improved with heliox, enabling it to be used as a diagnostic test.[4]

Helium containing gas mixtures are commonly used in deep water diving usually below a depth of 40m to

decrease the partial pressure of oxygen (minimising oxygen toxicity) and nitrogen (avoiding nitrogen narcosis) and to reduce the work of breathing associated with deep diving. Heliox is also used in decompression chambers to enable recompression to depths at which oxygen toxicity and/or nitrogen narcosis would otherwise occur.

The fact that helium is relatively insoluble in blood, at atmospheric pressure, enables its use in the assessment of functional residual capacity (FRC) via a helium dilution technique.

EFFECT OF HELIUM ON GAS EXCHANGE

Oxygen: Use of low density gases such as helium may lead to deterioration in gas exchange for reasons that are not immediately apparent. In a study by Christopherson *et al*,[47] changing from heliox to air in healthy subjects, with a constant FiO_2, resulted in a decrease in alveolar-arterial O_2 partial pressure difference. This is in contrast to the work of Schaeffer with intubated asthmatics.[30]

Carbon Dioxide: A number of studies have shown improved CO_2 clearance particularly during high frequency oscillation ventilation in paediatric patients.[48,49] However, if the tidal volume is held constant there is no change, suggesting that improvement is caused by increased tidal volumes for a given pressure.[50]

PROBLEMS IN THE USE OF HELIOX

At a practical level the majority of problems associated with the use of heliox are due to technical issues:

1. Helium may be difficult to obtain. In addition, there may be a significant time delay from time of ordering before supplies arrive;
2. In order to obtain real benefits in terms of decreased density, it is necessary to have a maximum FiO_2 of approximately 0.4;
3. Helium conducts heat 6 times faster than nitrogen. Patients breathing heliox for prolonged periods may require heated humidified circuits;
4. The different density of helium has a marked effect on the function of the valves within ventilators that control flow (see below);
5. Heliox is more expensive than air and oxygen. However, in comparison to other ICU treatments its cost is low.

USE OF HELIOX WITH CONVENTIONAL VENTILATORS

Flow through ventilator valves and tubing is typically turbulent, and for a given pressure, the lower the density of the inhaled gas the higher the flow.

This can potentially affect the delivered FiO_2 and tidal volumes. The FiO_2 is unaffected provided either

Table 3. Studies of the effect of heliox use on ventilator performance

Ventilator	Delivered FiO_2	Volume control mode Delivered Vt	Volume control mode Reported Vt	Pressure control mode Delivered Vt (vs FiO_2 1.0)	Pressure control mode Reported Vt
Veolar FT[51]	Accurate[51]	Higher than set[51]	Underestimated[51]	Unaffected[51]	
Galileo[51]	Accurate[51]	Higher than set[51]	Underestimated[51]	Unaffected[51]	
Evita 2[51]	Lower than set[51]	Higher than set[51]	Ventilator unable to monitor[51]	Unaffected[51]	
Evita 4[51,53]	Lower than set[51,53]	Higher than set[51,53]	Ventilator unable to monitor[51]	Unaffected[51,53]	
Servo 900C[51-53]	Accurate[51] Lower than set[52,53]	Higher than set[51-53]	Underestimated[51] Accurate[52]	Unaffected[51,52]	Underestimated[52]
Bear 1000[53]	Lower than set[53]	Higher than set [53]		Unaffected[53]	
Servo 300[51-53]	Accurate[51,52] Lower than set[53]	Accurate[51,53] Slightly lower than set[52]	Underestimated[51] Accurate[52]	Unaffected[51,53]	Slight overestimate[52]
Puritan Bennett 7200[51,53]	Much higher than set[51]	Markedly lower than set[51]	Ventilator unable to monitor[51,53]	Ventilator malfunctioned during testing[51]	
Bird VIP[52]	Lower than set[52]	Higher than set[52]	Overestimated[52]		Underestimated[52]
Bird VIP Gold[52]		Higher than set[52]	Underestimated[52]		Underestimated[52]

the mixing chamber is located upstream of the high-pressure gas inlet valves, as in the case of the Veolar (Hamilton Medical, Bonaduz AG, Switzerland), Galileo (Hamilton Medical) and Servo 900C (Siemens AG, Munich, Germany) ventilators, or there is a compensation mechanism, as in the Servo 300 (Siemens AG). The Evita 2 and 4 (Drager, Lubeck, Germany) and Bird (Bird Products Corp., Palm Spring, CA, USA) ventilators all have mixing chambers downstream from separate oxygen and air inlet valves, and there is a resulting discrepancy due to the higher than predicted flow of heliox through the air inlet, which is commonly used to allow the substitution of heliox for air.[51-53] The magnitude of the under-delivery of oxygen is inversely proportional to the FiO_2 (with FiO_2 delivered being an average of 10% lower with the Evita 2 and 4, reaching 18% at a FiO_2 set at 0.5).

Tidal volumes of helium delivered in the volume control mode tend to be higher than those set for the same reason, with the degree of discrepancy being inversely related to FiO_2. All ventilators (unless equipped with a compensatory mechanism as with the Servo 300) tend to be affected because the position of the mixing chamber is irrelevant.

The Puritan Bennett 7200 (Puritan-Bennett, Carlsbad, CA, USA) is an exception to the above. It over-delivers oxygen and there are large differences between predicted and observed tidal volumes. Although it has two high-pressure gas inlet valves (one for oxygen and one for air/heliox) with a downstream mixing chamber, the flow of gas through each inlet valve is measured by a hot wire pneumotachograph. This feeds back to adjust flow through the valves. Convective heat loss from the platinum wires of the pneumotachograph is higher with heliox (due to its 6 times greater thermal conductivity). This is interpreted as much higher flows than those set, and flow through the air/heliox inlet valve is consequently reduced. Since the oxygen valve is unaffected, there is an over-delivery of oxygen and a very large reduction in delivered volume. For this reason the Puritan Bennett 7200 cannot be used safely with heliox.[51]

Delivered tidal volumes in pressure control mode are generally unaffected compared to those delivered at FiO_2 of 1.0. This is due to the volume that is delivered being dependent on the mechanical properties of the lung. Flow through the ventilator inspiratory valves simply continues until the target pressure is reached.

Viasys (Viasys Healthcare, Conshohocken, PA, USA) have recently produced a ventilator (the Avea) that is specifically designed to administer heliox and features automatic compensation for the changes in gas density.

CONCLUSION

Coupled to its lack of biological activity, and almost instantaneous onset and offset, the physical properties of heliox make it a seemingly ideal temporising agent to reduce work of breathing in airway obstruction and allow standard therapies to take effect. Its low density is central to its ability to reduce the work of breathing and theoretically this should reduce the impact of respiratory muscle fatigue.

Heliox remains an attractive proposition for use in patients with upper airway obstruction. Anecdotally it has been associated with a reduction in the need for intubation in this clinical setting.

As for conditions in which lower expiratory airflow retardation is the primary problem, there is little firm evidence at this time that the use of heliox has any clinically significant benefit.

Until such time as evidence is obtained that demonstrates its efficacy in reducing clinically significant end-points it is not possible to recommend the routine use of heliox in either non-intubated or intubated patients with expiratory airflow retardation. Further work in the form of well-powered prospective, randomised clinical trails is required to demonstrate significant reduction in intubation rate, intensive care and hospital length of stay, as well as overall mortality rate in severe asthma and exacerbations of COPD.

The use of heliox with ventilators is also complicated by technical difficulties that result from those very same properties that are the basis of its potential benefit. Development of dedicated heliox capable ventilators (both for invasive and non-invasive ventilation), coupled with the ability to scavenge helium to reduce wastage and cost, should be a focus for industry.

In the meantime, the use of heliox remains indicated in conditions such as decompression illness as well as in investigative settings such as determining functional residual capacity.

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REFERENCES

1. www.york.ac.uk/depts/chem.
2. Wood L, Engel L, Griffin P. Effect of gas properties and flow on lower pulmonary resistance. J Appl Physiol 1974;41:234-244.
3. Jaber S, Carlucci A, Boussarsar M, et al. Helium-oxygen in the postextubation period decreases inspiratory effort. Am J Respir Crit Care Med 2001;164:633-637.

4. Weir M. Vocal cord dysfunction mimics asthma and may respond to heliox. Clin Pediatra (Phila) 2002;41:37-41.
5. Florin TH, Hills BA. Does counterperfusion supersaturation cause gas cysts in pneumatosis cystoids coli, and can breathing heliox reduce them? Lancet 1995;345:1220-1222.
6. Barr J, Eshel G, Chen-Levy Z, Lahat E. Heliox use in the treatment of hyperammonemia. J Child Neurol 2001;16:456-458.
7. Barach AL. The use of helium in the treatment of asthma and obstructive lesions in the larynx and trachea. Ann Intern Med 1935;9:739-765.
8. Grosz AH, Jacobs IN, Cho C, Schears GJ. Use of helium-oxygen mixtures to relieve upper airway obstruction in a pediatric population. Laryngoscope 2001;111:1512-4.
9. Connolly KM, McGuirt WF Jr. Avoiding intubation in the injured subglottis: the role of heliox therapy. Ann Otol Rhinol Laryngol 2001;110:713-717.
10. Khanlou H, Eiger G. Safety and efficacy of heliox as a treatment for upper airway obstruction due to radiation-induced laryngeal dysfunction. Heart Lung 2001;30:146-147.
11. Kemper KJ, Ritz RH, Benson MS, Bishop MS. Helium-oxygen mixture in the treatment of postextubation stridor in pediatric trauma patients. Crit Care Med 1991;19:356-359.
12. Polaner DM. The use of heliox and the laryngeal mask airway in a child with an anterior mediastinal mass. Anesth Analg 1996;82:208-210.
13. Weber JE, Chudnofsky CR, Younger JG, et al. A randomized comparison of helium-oxygen mixture (Heliox) and racemic epinephrine for the treatment of moderate to severe croup. Pediatrics 2001;107:E96.
14. Kass JE, Castriotta RJ. Heliox therapy in acute severe asthma. Chest 1995;107:757-760.
15. Martin-Barbaz F, Barnoud D, et al. The use of helium and oxygen mixtures in status asthmaticus. Rev Pneumol Clin 1987;43:186–189.
16. Shiue ST, Gluck EH. The use of helium-oxygen mixtures in the support of patients with status asthmaticus and respiratory acidosis. J Asthma 1989;26:177–180.
17. Rose JS, Panacek EA, Miller P. Prospective randomized trial of heliox-driven continuous nebulizers in the treatment of asthma in the emergency department. J Emerg Med 2002;22:133-137.
18. Kress JP, Noth I, Gehlbach BK, Barman N, Pohlman AS, Miller A, Morgan S,Hall JB. The utility of albuterol nebulized with heliox during acute asthma exacerbations. Am J Respir Crit Care Med 2002;165:1317-1321.
19. Bag R, Bandi V, Fromm RE Jr, Guntupalli KK. The effect of heliox-driven bronchodilator aerosol therapy on pulmonary function tests in patients with asthma. J Asthma 2002;39:659-665.
20. Henderson SO, Acharya P, Kilaghbian T, Perez J, Korn CS, Chan LS. Use of heliox-driven nebulizer therapy in the treatment of acute asthma. Ann Emerg Med 1999;33:141-146.
21. Dorfman TA, Shipley ER, Burton JH, Jones P, Mette SA. Inhaled heliox does not benefit ED patients with moderate to severe asthma. Am J Emerg Med 2000;18:495-497.
22. Kass JE, Terregino CA. The effect of heliox in acute severe asthma: a randomized controlled trial. Chest 1999;116:296-300.
23. Carter ER, Webb CR, Moffitt DR. Evaluation of heliox in children hospitalized with acute severe asthma. A randomized crossover trial. Chest 1996;109:1256-1261.
24. Kudukis TM, Manthous CA, Schmidt GA, Hall JB, Wylam ME. Inhaled helium-oxygen revisited: effect of inhaled helium-oxygen during the treatment of status asthmaticus in children. J Pediatr 1997;130:217-224.
25. Manthous CA, Hall JB, Caputo MA, Walter J, Klocksieben JM, Schmidt GA, Wood LD. Heliox improves pulsus paradoxus and peak expiratory flow in nonintubated patients with severe asthma. Am J Respir Crit Care Med 1995;151(2 Pt 1):310-314.
26. Hess DR, Acosta FL, Ritz RH, Kacmarek RM, Camargo CA. The effect of heliox on nebuliser function using a β-Agonist Bronchodilator. Chest 1999;115:184-189.
27. Rodrigo G, Pollack C, Rodrigo C, Rowe B. Heliox for nonintubated acute asthma patients. Cochrane Database Syst Rev. 2003;4. CD002884. Review
28. Ho AM, Lee A, Karmakar MK, Dion PW, Chung DC, Contardi LH. Heliox vs air-oxygen mixtures for the treatment of patients with acute asthma: a systematic overview. Chest 2003;123:882-890.
29. Rodrigo GJ, Rodrigo C, Pollack CV, Rowe B. Use of helium-oxygen mixtures in the treatment of acute asthma: a systematic review. Chest 2003;123:891-896
30. Schaeffer EM, Pohlman A, Morgan S, Hall JB. Oxygenation in status asthmaticus improves during ventilation with helium-oxygen. Crit Care Med 1999;27:2666-2670.
31. Gluck EH, Onorato DJ, Castriotta R. Helium-oxygen mixtures in intubated patients with status asthmaticus and respiratory acidosis. Chest 1990;98:693-698.
32. de Boisblanc BP, DeBleiux P, Resweber S, Fusco EE. Randomized trial of the use of heliox as a driving gas for updraft nebulization of bronchodilators in the emergency treatment of acute exacerbations of chronic obstructive pulmonary disease. Crit Care Med 2000;28:3177-3180.
33. Swidwa DM, Montenegro HD, Goldman MD, Lutchen KR, Saidel GM. Helium-oxygen breathing in severe chronic obstructive pulmonary disease. Chest 1985;87:790-795.
34. Pecchiari M, Pelucchi A, D'Angelo E, Foresi A, Milic-Emili J, D'Angelo E. Effect of heliox breathing on dynamic hyperinflation in COPD patients. Chest 2004;125:2075-2082.
35. Gerbeaux P, Gainnier M, Boussuges A, Rakotonirina J, Nelh P, Torro D, Arnal JM, Jean P. Use of heliox in patients with severe exacerbation of chronic obstructive pulmonary disease. Crit Care Med 2001;29:2322-2324.

36. Maggiore SM, Richard JC, Diehl JL, Abroug F, Lecourt L, Brochard L. Effect of helium-oxygen during non-invasive ventilation (NIV) for acute exacerbation of hypercapnic respiratory failure. AJRCCM 2005;A812.
37. Jolliet P, Tassaux D, Roeseler J, et al. Helium-oxygen versus air-oxygen noninvasive pressure support in decompensated chronic obstructive disease: A prospective, multicenter study. Crit Care Med 2003;31:878-884.
38. Jolliet P, Tassaux D, Thouret JM, Chevrolet JC. Beneficial effects of helium:oxygen versus air:oxygen noninvasive pressure support in patients with decompensated chronic obstructive pulmonary disease. Crit Care Med 1999;27:2422-2429.
39. Jaber S, Fodil R, Carlucci A, et al. Noninvasive ventilation with helium-oxygen in acute exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2000;161(4 Pt 1):1191-1200.
40. Tassaux D, Jolliet P, Roeseler J, Chevrolet JC. Effects of helium-oxygen on intrinsic positive end-expiratory pressure in intubated and mechanically ventilated patients with severe chronic obstructive pulmonary disease. Crit Care Med 2000;28:2721-2728.
41. Diehl JL, Mercat A, Guerot E, et al. Helium/oxygen mixture reduces the work of breathing at the end of the weaning process in patients with severe chronic obstructive pulmonary disease. Crit Care Med 2003;31:1415-1420.
42. Rodrigo G, Pollack C, Rodrigo C, Rowe B. Heliox for treatment of exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2002;(2) CD003571. Review.
43. Martinon-Torres F, Rodriguez-Nunez A, Martinon-Sanchez JM. Heliox therapy in infants with acute bronchiolitis. Pediatrics 2002;109:68-673.
44. Hollman G, Shen G, Zeng L, et al. Helium-Oxygen improves clinical Asthma Scores in children in acute bronchiolitis. Crit Care Med 1998;26:1731-1736.
45. Gross MF, Spear RM, Peterson BM. Helium-oxygen mixture does not improve gas exchange in mechanically ventilated children with bronchiolitis. Crit Care 2000;4:188-192.
46. Ahmedzai SH, Laude E, Robertson A, Troy G, Vora V. A double blind, randomised, controlled Phase II trial of heliox28 gas mixture in lung cancer patients with Dyspnoea on exertion. Br J Cancer 2004;90:366-371.
47. Christopherson SK, Hlastala MP. Pulmonary gas exchange during altered density gas breathing. J Appl Physiol 1982;52:221-225.
48. Katz A, Gentile MA, Craig DM, et al. Heliox improves gas exchange during high-frequency ventilation in a pediatric model of acute lung injury. Am J Respir Crit Care Med 2001;164:260–264.
49. Winters JW, Willing MA, Sanfilippo D. Heliox improves ventilation during high-frequency oscillatory ventilation in pediatric patients. Pediatr Crit Care Med 2000;1:33–37.
50. Katz AL, Gentile MA, Craig DM, Quick G, Cheifetz IM. Heliox does not affect gas exchange during high-frequency oscillatory ventilation if tidal volume is held constant. Crit Care Med 2003;31:2006-2009.
51. Tassaux D, Jolliet P, Thouret JM, Roeseler J, Dorne R, Chevrolet JC. Calibration of seven ICU ventilators for mechanical ventilation with helium-oxygen mixtures. Am J Respir Crit Care Med 1999;160:22-32.
52. Berkenbosch JW, Grueber RE, Dabbagh O, McKibben AW. Effect of helium-oxygen (heliox) gas mixtures on the function of four pediatric ventilators. Crit Care Med 2003;31:2052-2058.
53. Oppenheim-Eden A, Yitzhak C, Weissman C, Pizov R. The effect of helium on ventilator performance. Study of five ventilators and a bedside pitot tube spirometer. Chest 2001;120:582-588.