Validation of volume delivery with the use of heliox in mechanical ventilation

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Abstract. Using a mixture of helium and oxygen (heliox) while mechanically ventilating patients to relieve lower airway obstruction is commonly practiced in intensive care units. The use of heliox with commercially available mechanical ventilators is usually accomplished by connecting the heliox mixture to the air inlet of the ventilator. Since most ventilators do not compensate for the difference in gas densities, particular attention to the delivered tidal volume (V_T) is required. We utilized a commercially available mechanical ventilator with an internal blending system that is capable of delivering heliox instead of medical air. It identifies and compensates for the gas mixture, theoretically enhancing stability in delivered and monitored parameters. Intubated, sedated male domestic pigs ($n = 7$) were ventilated with a mechanical ventilator equipped with an internal heliox blending system utilizing pressure assist control, pressure regulated volume control, and pressure support ventilation modes. Accuracy of volume delivery was assessed by comparing delivered V_T measured at the patient wye using the variable orifice flow sensor connected to the ventilator and a heated 0–35 L/min pneumotachograph that was calibrated for flow, pressure, and volume, with a 0.80/0.20 heliox mix and 0.50 oxygen. A paired t-test was utilized with a $P < 0.05$. Pigs mean weight 9.0 ± 0.9 kg. Mean exhaled tidal volume for all modes and was 66 ± 16 mL. When comparing all modes for the 0.50 oxygen to the heliox mix, we found that exhaled tidal volume % difference increased when using heliox ($P \leq 0.037$). This study confirms that clinicians should be vigilant in monitoring delivered V_T using a commercially available ventilator equipped with an internal heliox blending system. Accuracy of delivered V_T can vary greatly with the use of heliox in this system, as well as other configurations.

Keywords: Pediatric, critical care, artificial respiration, monitoring, ventilation

1. Introduction

Heliox is a combination of oxygen (O_2) and helium 1st described in 1934 as a treatment for asthma [1]. Helium is an inert gas with low density and molecular weight that does not interact with body tissues or fluids.

Its physical properties allow it to flow through airways with less turbulence than air or O_2 [2]. By reducing turbulent gas flow, a mixture of helium and O_2 can carry aerosol medications further into the airways than air or O_2 alone, thus improving bronchodilation [3,4], ventilation, respiratory acidosis, and oxygenation [5]. Since its first use as treatment for asthma, clinical applications have expanded to include other etiologies of airway obstruction such as post-extubation stridor, croup, bronchiolitis [2], and chronic obstructive pulmonary disease exacerbations [6].

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Prospective and retrospective studies with heliox have shown beneficial effects during mechanical ventilation for patients with lower-airway obstruction [7]. One such study looked at children with asthma exacerbations requiring mechanical ventilation and found significant decreases in mean peak inspiratory pressure (PIP) and mean PaCO_2 after initiation of heliox [8]. However, delivery of heliox through a ventilator can be challenging. To use heliox with most commercially available ventilators, the heliox mixture is connected directly to the air inlet on the ventilator. However, helium interferes with ventilator function and with accuracy of the pneumotachometer [7], and the lower gas density causes inaccurately high readings from flow meters calibrated for air and/or O_2 [9]. Multiple studies have examined heliox delivery with commercially available ventilators and found that delivered tidal volume (V_T) was different than set V_T in almost all ventilators tested [10–12]. However, one ventilator, the CareFusion Avea (CareFusion Corp., San Diego, CA), has an internal blending system that allows for heliox delivery that has not had data published regarding volume accuracy to date. This ventilator is different from other commercially available ventilators because it identifies and compensates for the low density gas mixture of O_2 and helium, theoretically enhancing stability in delivered and monitored parameters. We assessed the accuracy of volume delivery with this new system. Our hypothesis was that the accuracy of volume delivery would be improved with the use of an internal ventilator-controlled compensation for helium- O_2 delivery.

2. Materials and methods

The Animal Review Committee of the University of Arkansas for Medical Sciences approved this study. Animals were cared for in accordance with the standards for care and use of laboratory animals set forth by the University and the National Institutes of Health guidelines for principles of laboratory animal care.

2.1. Animal methods

Studies were performed on seven male pigs (weight 9.0 ± 0.9 kg). Pigs were anesthetized with forane (3.5–4%) for approximately 5 min via a special veterinary inhalation mask and then intubated with a 4.5–5.5 mm inner diameter cuffed endotracheal tube. Endotracheal tube location was confirmed by direct visualization, and the

cuff was inflated to a minimal occlusive pressure. Catheters were surgically placed in the external jugular vein for drug administration. Midazolam (0.3 mg/kg/h), propofol (3 mg/kg/h), and when indicated, succinylcholine (2 mg/kg) were administered intravenously for sedation and neuromuscular blockade, respectively.

The pigs were ventilated with the Avea ventilator in separate tests utilizing FiO_2 of either 0.80/0.20 heliox mix or 0.50 O_2 in three different modes of ventilation: Pressure assist control (P A/C), pressure regulated volume control and pressure support ventilation (PSV). Other ventilator settings were set respiratory rate (when applicable) of 30 beats per min, set V_T (when applicable) of 6–8 mL/kg, set PIP (when applicable) to get 6–8 mL/kg of V_T , and set positive end expiratory pressure of 5 cmH₂O (control mode) or 2 cmH₂O (support mode). Pigs were ventilated in a prone position. Gas humidification was maintained by an in-line Fisher & Paykel humidification system with temperature set at 37°C. Heart rate, pulse oximeter saturation, and temperature were monitored continuously with a physiologic monitor. The heliox option on the Avea ventilator is only available while utilizing the variable orifice flow sensor.

2.2. Data acquisition

Measurements of respiratory flow and pressure waveforms were acquired using the Biopac MP-100 System (Biopac Systems, Inc, Aero Camino Goleta, CA). A heated 0–35 L/min pneumotachograph (Hans Rudolph, Inc., Shawnee, KS) was placed in line, at the patient wye, between the endotracheal tube and the ventilator. The pneumotachograph flow was calibrated with heated and humidified gas of either 0.80/0.20 heliox mix or 0.50 O_2 for the corresponding studies. Volume measurements were obtained through the computer by integrating the flow signal. Volume was verified with a calibrated syringe (Hans Rudolph, Inc., Shawnee, KS), using heated, humidified gas of the appropriate gas mixture. Pressure was calibrated with a water column manometer. All output signals were routed via an analog channel box into the Biopac MP100 data acquisition unit converting them into digital signals that can be processed with a computer. Signals were obtained at a rate of 1000 samples per sec.

2.3. Volume accuracy

Displayed inspired tidal volume and exhaled tidal volume (V_{TE}) were recorded (via video) from the Avea

screen and compared to the data acquired from the pneumotachograph at the airway opening. Data recorded from the Avea screen were 10 consecutive breaths matched (time wise) to the same 10 consecutive breaths collected from the pneumotachograph at the airway opening. Methods were previously described by Heulitt et al. [13]. PIP, peak flow and mean airway pressure were also collected.

2.4. Statistical analysis

A parametric paired t-test was utilized for analysis ($P < 0.05$). We found similar results with Wilcoxon Signed Ranks Test. Bland-Altman plots were constructed as the difference vs. the V_{TE} mean between the ventilator-displayed V_{TE} and the V_{TE} measured by the pneumotachograph at the airway. The difference, or bias, is calculated as the mean difference in the ventilator- displayed V_{TE} and the pneumotachograph measured V_{TE} , and precision is the variance or standard deviation. With Bland-Altman plots, we expect to see random scatter about zero (i.e., no difference between

the measurements from the two methods) and uniform variability throughout the range of measurements.

3. Results

Pigs mean weight was 9.0 ± 0.9 kg. Mean V_{TE} was 66 ± 16 mL for both FiO_2 0.5 and heliox 0.80/0.20 mix across all modes. Mean V_{TE} % difference $\pm$ SD and V_{TE} difference/kg are shown in Table 1. When comparing all modes for the 0.50 O_2 to the heliox mix, we found that V_{TE} % difference increased when using heliox ($P \leq 0.037$). We also found no difference in PIP and mean airway pressure when comparing 0.50 O_2 to the heliox mix (Table 2). However, there was an increase in peak flow for P A/C and PSV modes with the use of the heliox mix (Table 2).

Bland-Altman plots are shown in Figs. 1 and 2 for both the 0.50 O_2 and the heliox mix. For the 0.50 O_2 plot, there is less scatter for pressure regulated volume control and P A/C than for PSV. The heliox plot has a larger bias and shows more scatter, across all modes, and greater variance when compared to the 0.50 O_2 plot.

Table 1
Mean, V_{TE} % difference and V_{TE} difference mL/kg $\pm$ SD for each mode of ventilation

	Mode	0.50 FiO_2	0.80/0.20 heliox	P value
V_{TE} % difference	Pressure regulated volume control	6.5 ± 12.2	16.7 ± 17.9	< 0.001
	Pressure assist control	5.9 ± 7.7	20.3 ± 21.1	< 0.001
	Pressure support ventilation	9.2 ± 11.7	14.3 ± 12.3	0.037
V_{TE} difference/kg	Pressure regulated volume control	0.4 ± 0.8	1.4 ± 1.4	< 0.001
	Pressure assist control	0.4 ± 0.5	1.9 ± 2.1	< 0.001
	Pressure support ventilation	0.7 ± 0.9	1.5 ± 1.2	< 0.001

Table 2
Mean peak inspiratory pressure, peak flow and mean airway pressure $\pm$ SD for each mode of ventilation

	Mode	0.50 FiO_2	0.80/0.20 Heliox	P value
Peak inspiratory pressure (cm H_2O)	Pressure regulated volume control	13.0 ± 1.3	12.6 ± 1.2	NS
	Pressure assist control	13.0 ± 1.4	13.5 ± 0.7	NS
	Pressure support ventilation	6.3 ± 2.0	5.9 ± 1.5	NS
Peak flow (mL/s)	Pressure regulated volume control	181.0 ± 31.9	208.1 ± 48.2	NS
	Pressure assist control	140.3 ± 18.8	165.6 ± 18.5	0.008
	Pressure support ventilation	170.2 ± 34.9	186.1 ± 33.5	0.024
Mean airway pressure (cm H_2O)	Pressure regulated volume control	7.8 ± 0.3	8.0 ± 0.5	NS
	Pressure assist control	7.8 ± 0.3	8.3 ± 0.7	NS
	Pressure support ventilation	3.1 ± 0.4	3.1 ± 0.4	NS

NS = Not significant.

Fig. 1. Variable orifice flow sensor with FiO₂ set 0.50 - Bland-Altman plots were constructed as the V_T difference versus the V_T mean between the ventilator displayed/set V_T and the V_T measured by the pneumotachograph at the airway. Zero (solid line), mean (small dash) and $\pm$ 2SD (long dash) are shown.

VOF = Variable orifice flow sensor; PRVC = pressure regulated volume control; Pressure A/C = Pressure assist control; PSV = Pressure support ventilation; VTE = Exhaled tidal volume.

Fig. 2. Variable Orifice Flow Sensor (VOF) with 0.80/0.20 Heliox - Bland-Altman plots were constructed as the V_T difference versus the V_T mean between the ventilator displayed/set V_T and the V_T measured by the pneumotachograph at the airway. Zero (solid line), mean (small dash) and $\pm$ 2SD (long dash) are shown.

VOF = Variable orifice flow sensor; PRVC = pressure regulated volume control; Pressure A/C = Pressure assist control; PSV = Pressure support ventilation; VTE = Exhaled tidal volume.

4. Discussion

Our study concludes that delivered V_T is unreliable when using heliox with mechanical ventilation, which is consistent with the findings of previous studies [10–12]. The primary difference between our study and the prior studies is that the ventilator tested, the CareFusion Avea, claims to accurately deliver heliox using an internal blending system. However, our study shows delivered V_T continues to be inaccurate, with V_{TE} % difference significantly increased when using heliox ($P \leq 0.037$). In contrast, an abstract presented in 2003 found no significant difference in volume delivery using varying modes of ventilation with this ventilator with and without heliox. The raw data suggest differences in V_T delivery, but these differences were not deemed clinically significant in their study [14].

All previous studies looking at heliox delivery in mechanical ventilation compared accuracy of FiO_2 delivery, which we did not test. They also utilized test lung models for their experiments [10–12]; however, we used a live animal model with pediatric-sized pigs for this study. Our method has been used in our previous studies looking at volume accuracy in both animals and children with good results [13,15]. Utilizing animals provides a more realistic approximation of inspiratory flow rates, inspiratory times, and V_T delivery in patients than test lungs.

One limitation of our study is that we used a small number of animals ($n = 7$). Expanding numbers would improve the power of our study. In addition, we compared a 0.80/0.20 heliox mix and 0.50 O_2 . It could be argued that we should have compared the 0.80/0.20 heliox mix to 0.20 O_2 for equal O_2 delivery. However, while we could have selected a lower FiO_2 , it is more common for patients to require greater than 0.21 O_2 while being mechanically ventilated. We could also expand our study to evaluate different concentrations of helium, measure FiO_2 accuracy as previous studies have done, and use multiple Avea ventilators to assess inter-ventilator reliability.

During volume ventilation, delivered V_T is calculated from inspiratory time and gas flow rate. Previous authors have concluded that heliox flow rates will be greater than expected because of the decreased density, and V_T delivery will thus be increased [10]. Most flow sensors are not calibrated to heliox, they are calibrated to air and/or O_2 , so differences between set V_T , delivered V_T and V_{TE} can be expected [11]. However, we postulate that the internal blending system of the Avea

is still inadequate to compensate for the decreased density of heliox allowing for continued increased flow rates.

The clinical implications of this study are important because the advertised internal algorithm for adjusting volume delivery with the use of heliox in the Avea may be inadequate. Clinicians using this ventilator may be unaware of this discrepancy and cause lung injury by delivering excess V_T . One important goal of ventilation in infants and children is prevention of overdistention by limiting V_T and avoiding volutrauma [16,17]. Alveolar overdistention has been recognized as the primary determinant of ventilator-associated lung injury. The use of lower V_T may improve mortality and ventilator-free days [18]. Knowing exact inspired and expired gas volume is thus vital for optimizing ventilator settings [15] and avoiding lung injury.

In conclusion, our study demonstrates that a ventilator designed with a heliox delivery system has inaccurate measurement of V_T delivery. Knowing exactly how much V_T is delivered to patients is important for minimizing ventilator-induced lung injury.

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