

Title: Effect of Heliox on End-tidal CO₂ Measurement in Healthy Adults

Keywords: Capnography, end-tidal CO₂, heliox.

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ABSTRACT

Purpose: Therapeutic gases and other modalities delivered by inhalation may affect the accuracy of capnographic measurements in two ways. First is the specificity of the measurement of CO₂ within the device and second is the dilution effect of supplemental gases in the ambient air during CO₂ sampling by the device. Our goal was to determine if variables such as inhaled gas composition, variable gas flow rates delivered via non-rebreather mask, and mouth position affect this technology's capnographic measurements of end-tidal CO₂ pressure (PetCO₂). **Methods:** We measured PetCO₂ and RR by capnography in 20 adult normal volunteers with coaching to maintain their respiratory frequency between 10-20 bpm. Arterial oxygen saturation was monitored to detect hypoxemia. A six minute washout period occurred between each six minute level of testing. **Results:** A mixed models analysis revealed that the average PetCO₂ for all subjects and flow rates while breathing heliox, 36.9+/-4.5 mm Hg (mean+/-SD), was not different ($p = 0.501$) from the value while breathing room air, 36.0+/-4.5 mm Hg. Repeated measurements on each of the same subjects over 6 minute periods of breathing spontaneously 0 L/min, with 10 L/min flow rate, and with 15 L/min flow rate of either air or heliox showed no difference in PetCO₂ related to flow (0 L/min vs. 10 L/min, $p = 0.759$; 0 L/min vs. 15 L/min, $p=0.642$; 10 L/min vs. 15 L/min, $p=0.865$). **Conclusions:** It appears that PetCO₂ measurements in normal subjects are not affected by heliox or gas flow at 10 or 15 L/min through a non-rebreathing mask with this device.

Introduction

Capnography provides a means to assess alveolar ventilation, the integrity of the airway, and ventilatory function by measuring the partial pressure of exhaled carbon dioxide throughout the breathing cycle. Carbon dioxide (CO_2), as a product of cellular metabolism, is carried in deoxygenated blood to pulmonary capillaries where CO_2 diffuses into the alveolar space for exhalation while oxygen diffuses into the blood as a function of the partial pressure gradient across the alveolar-capillary membrane of each gas. In addition to ventilation and gas exchange, changes in perfusion affect the relationship between arterial CO_2 and PetCO_2 (this effect is minimized with healthy subjects).

A variety of inspired gases (oxygen, helium, nitrous oxide, etc.) can affect the accuracy of capnography devices.¹⁻³ Oxygen can be mixed with helium to enhance its delivery to the alveoli in some cases of partial airway obstruction. Helium is a nontoxic, biologically inert gas of low molecular weight that has no bronchodilating or anti-inflammatory properties.⁴⁻⁵ The low density of helium allows it to pass through the airways with less turbulence thereby reducing the work of breathing in patients with severe airway obstruction. The high diffusion coefficient of helium allows CO_2 to diffuse more rapidly than through air or oxygen thereby improving CO_2 elimination from the lungs.⁶ In addition, elimination of CO_2 is also improved with the lower pressure per unit volume of heliox due to the lower specific gravity of helium which also produces a reduction in auto-PEEP and reduction in dynamic with a resultant reduction in physiologic deadspace.

The first therapeutic use of a helium-oxygen mixture in 1934 by Alvin Barach to relieve dyspnea in patients with upper airway obstruction during asthma exacerbations.⁷ Recent clinical studies have focused on using heliox as the driving gas for nebulizing β_2 agonist bronchodilators to assess improved aerosol delivery to the smaller airways.⁸ Patients requiring heliox are at risk of ventilatory compromise and therefore careful monitoring of ventilation during delivery of supplemental heliox is important to detect hypercapnia and hypoxemia due to the limit of oxygen amount in heliox of not more than 30%.

Monitoring of oxygenation and ventilation includes continuous pulse oximetry and capnography as well as arterial blood gas analysis. Oridion Capnography Inc. (now Covidien Inc., Boulder, CO), purports to have a CO₂ sensing technology that is unaffected by heliox and anesthesia gases and minimal dilution of the CO₂ sample by supplemental gases delivered by the CO₂ sampling Filterline®. Our aim was to determine if the presence of heliox or differences in flow rate of inspired gas affect the accuracy of PetCO₂ either through sampling dilution or precision of the technology when heliox is provided via the standard non-rebreather mask at a therapeutic concentration and flow in healthy people with no ventilation or perfusion abnormalities.

Methods

This pilot project used a pretest and posttest design to determine the effects of various gas flow rates and heliox through a nonrebreathing mask on measured PetCO₂. After obtaining IRB approval for this study, twenty healthy volunteers were recruited to participate. An IRB-approved advertisement was placed within the School of Health Professions in key areas

(student and faculty lounges, near elevators and internal department postings) to recruit healthy participants between the ages of 19-55 years of age. After obtaining consent from the healthy adult volunteers, normal lung function was measured by spirometry (normal FEV₁, FVC, and FEV₁%) using NHANES III predicted normal equations. Any participant with an abnormal pulmonary status as demonstrated by spirometry, a history of lung disease (asthma, cystic fibrosis, interstitial lung disorders, chronic obstructive pulmonary disease, and others), an oral temperature of $\geq 100^{\circ}\text{F}$ (37.8°C), or employees from the Department of Respiratory Care were excluded. There was no review of medical charts or contact with an individual's private physician to determine if lung disease exists. All consented patients actively enrolled in this study received a gift card worth twenty-five dollars in compensation for their time.

The participants were given sequential ID numbers to remain anonymous. The following baseline participant data were recorded: patient demographics (age, gender, ethnicity), lung health history, spirometry values (EasyOne, ndd Medical Technologies Inc., Andover, MA), noninvasive measurement of pulse rate (PR) and arterial hemoglobin oxygen saturation via Oximax pulse oximeter (SpO₂), PetCO₂, CO₂-derived respiratory frequency (RR) via Capnostream 20, manual respiration rate and patient temperature (via electronic thermometer). Environmental conditions of ambient temperature, humidity, and barometric pressure were recorded. The Capnostream 20 (Oridion Capnography Inc., now Covidien Inc., Boulder, CO) monitors were verified to be in calibration by the manufacturer immediately prior to data collection and according to the manufacturer's directions for use. No participant had difficulty breathing or reported feeling uncomfortable.

The following study procedures were followed for each participant after the consent procedure was completed. The Capnostream 20 non-invasive OxiMax SpO₂ finger probe was placed on the participant's finger to monitor oxygenation. A single patient use non-invasive oral/nasal CO₂ sampling filterline was connected to the Oridion monitor and placed on the participant with the sampling cannula in the nares and over the mouth. Correct placement of the CO₂ sampling filterline by visual inspection was verified by one of the investigators before each six minute test period. The participant ID number was entered into the monitor and electronic data capture of the CO₂ waveform was started in parallel with manual recording on the case record form by study staff. Baseline (no mask) data were recorded on air room conditions for six minutes. A non-rebreather mask was placed on the participant's face and a good fit was verified. The gases (room air or heliox-80% helium/20% oxygen) and gas flow rates (10 L/m or 15 L/m) were provided in a random order using a randomization table. A heliox regulator with flow gauge was used to control proper helium flow rate. The participants were also blinded to the gas and flow rate they received. The gases were hidden behind a curtain to prevent participants from seeing what type of gas was being delivered and the set flow rate. The participants were required not to talk and viewed a movie during the six minutes of data capture. The participants were coached to maintain a normal respiratory rate (12-20 breaths/min) throughout the experiment. The nonrebreather mask was removed for six minutes after each six minute measurement period to flush residual effects of the previous gas flow from the lungs with ambient room air.

The first study question sought to determine if gas mixture, flow rate, or mouth position produced a difference in measured PetCO₂. Two methods were used to evaluate differences 1) bivariate analyses—tests of mean differences in the five measured variables of interest for the conditions of gas mixture, flow rate, and mouth position, and 2) multivariable models—for each of the five measured variables a linear mixed model was fitted with the explanatory variables age, gender, time, gas mixture, flow rate, and mouth position, as well as the interactions gas mixture x flow rate, gas mixture x mouth position, and flow rate x mouth position. This included a covariance structure that accounts for statistical dependence among the repeated measures on the same individuals, as well as a lack of homogeneity of variance/covariance between the gas mixture, flow rate, and mouth position combinations. Statistical significance was based upon an alpha level of 0.05 and analysis was performed with SAS® statistical software, version 9.2.

Results

This group of 20 healthy adult participants (75% female) ranged in age from 20-36 years (25.8±4.7 yr. mean±SD) and was comprised of 10% Asian, 5% African-American, 20% Caucasian, and 65% identifying as “other.” The descriptive statistics for gas mixture effect (air vs. 80/20 heliox) and the summary results for the tests of mean differences by gas mixture and flow rates are given in Table 1. The means for each variable are provided with the p-values to facilitate determination of clinical and statistical significance. There were no statistically or clinically significant differences between the measured PetCO₂ for all the conditions of gas composition and flow tested. The mean differences with standard deviation data for mouth position are

provided in Figure 1. The descriptive and inferential statistics both indicate that the different gas mixtures, flow rates, and mouth positions produced no significant differences in the PetCO₂.

Discussion

Breathing heliox caused no difference in PetCO₂ and derived RR measurement using a Capnostream 20 monitor during resting breathing in this group of young adults with normal spirometry. These same measurements were not affected by differing flow rates of heliox or ambient air compared to breathing with no mask. The different gas administration levels represent variations commonly employed in clinical practice and were important to achieve greater confidence in being able to generalize the findings.

Heliox is used in the clinical setting to lower work of breathing in patients with severe obstruction and could be used in conjunction with capnography monitoring, both for intubated and non-intubated patients. Because of the potential for co-incident use of these modalities and the previously described reports of gases affecting earlier capnography technology, it is important to verify the manufacturer claims that the Capnostream 20 accuracy is unaffected by heliox. The lack of effect is attributed to the proprietary Molecular Correlation Spectroscopy laser-based technology that produces a precise infrared emission that matches carbon dioxide's absorption spectrum.

Different levels of gas flow were included in the testing schema to better represent the typical variations seen in the clinical setting. The greater the flow administered to participants, the more likely the accuracy could be affected, so two robust flow rates were compared to measurements at zero gas flow. Likewise, capnography sampling devices must be able to

handle the variability of a user's mouth position alternating between open and closed. The results of this sample indicate that the oral/nasal sampling cannula was effective at capturing consistent measurements, regardless of whether the user is breathing by nose or mouth.

There are limitations to this study, the first being the fact that the study population was comprised of healthy participants with no cardiopulmonary disease that could alter deadspace or the relationship between arterial and end-tidal CO₂. Secondly, this was a small pilot study completed in a controlled environment. These findings need to be confirmed in a patient population that requires high gas flows and/or heliox through a non-rebreather mask.

In conclusion, differences in helium concentration, gas flow rate, and mouth position did not affect the accuracy of PetCO₂ measurement by the Capnostream 20 in healthy volunteers. These findings have practice implications for both intubated and non-intubated patients receiving heliox in emergent and critical care settings. This medical gas is usually used in patients with a high acuity which further establishes the need to continually monitor them for increasing PetCO₂ and possible respiratory failure. Other critically ill patients receiving oxygen through a non-breather mask also have a need for accurate noninvasive ventilation measurements to guide support and treatment. Further investigation of this new capnography technology with high oxygen concentrations and nitrous oxide is merited to determine its susceptibility to these variables.

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Figure 1. Mouth position effect on PetCO₂ (error bars represent standard deviation estimated with mixed models to account for the covariance among the repeated measurements on the same participant). No difference as a result of mouth position found using bivariate analysis.

Table 1. Bivariate Tests of Mean Differences for Gas Mixture and Supplemental Flow Rate Effects.

Condition	PetCO ₂ (Mean±SD)	p-value
Air (all)	36±5	0.50 Air vs. Heliox
Heliox (all levels)	37±5	
No Mask (0 L/min)	37±4	0.75 0 vs. 10 L/min
Mask at 10 L/min	36±4	0.63 0 vs. 15 L/min
Mask at 15 L/min	36±5	

*Mixed models used to account for covariance among repeated measurements on same participants.

