Comparing the EMMA capnograph with sidestream capnography and arterial carbon dioxide pressure at 284 kPa

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Abstract
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Introduction: Capnography aids assessment of the adequacy of mechanical patient ventilation. Physical and physiological changes in hyperbaric environments create ventilation challenges which make end-tidal carbon dioxide ($ETCO_2$) measurement particularly important. However, obtaining accurate capnography in hyperbaric environments is widely considered difficult. This study investigated the EMMA capnograph for hyperbaric use.

Methods: We compared the EMMA capnograph to sidestream capnography and the gold standard arterial carbon dioxide blood gas analysis in a hyperbaric chamber. In 12 resting subjects breathing air at 284 kPa, we recorded $ETCO_2$ readings simultaneously derived from the EMMA and sidestream capnographs during two series of five breaths (total 24 measurements). An arterial blood gas sample was also taken simultaneously in five participants.

Results: Across all measurements there was a difference of about 0.1 kPa between the EMMA and sidestream capnographs indicating a very slight over-estimation of $ETCO_2$ by the EMMA capnograph, but fundamentally good agreement between the two end-tidal measurement methods. Compared to arterial blood gas pressure the non-significant difference was about 0.3 and 0.4 kPa for the EMMA and sidestream capnographs respectively.

Conclusions: In this study, the EMMA capnograph performed equally to the sidestream capnograph when compared directly, and both capnography measures gave clinically acceptable estimates of arterial PCO_2.

Introduction

End-tidal carbon dioxide monitoring is vital when monitoring mechanically ventilated patients to ensure adequate ventilation.[1] This applies to patients in intensive care, but potentially more so during treatment inside a hyperbaric chamber due to physiological and pressure changes[2] which frequently necessitate adjustments to ventilator parameters.[3] Unfortunately, not all technology can be brought into the hyperbaric chamber environment due to physical incompatibilities (like pressure and temperature), electrical power restrictions and increased fire risks.[4]

Capnography aims to measure the pressure of carbon dioxide (PCO_2) in the expired gas at the end of each exhalation (the end-tidal CO_2 [$ETCO_2$]). This is accepted as an adequate surrogate for the PCO_2 in arterial blood. The sensors used for measuring CO_2 in this context are typically spectroscopic and discern CO_2 molecules by their characteristic absorption of infrared light. These sensors can be deployed in mainstream or sidestream configurations. Mainstream positioning puts the sensor in the main flowpath for exhaled and inhaled gas at the end of the endotracheal tube. Sidestream positioning puts the sensor outside the main flowpath, with a continuous gas sample drawn from the end of the endotracheal tube to the sensor via a narrow bore tube. In the hyperbaric setting the sidestream capnography sensor is commonly placed outside the chamber, with the sampling line ported through the chamber wall. The pressure difference during the hyperbaric treatment will force gas through the tubing. The PCO_2 measurements made at normobaric pressure need to be multiplied by the absolute pressure inside the chamber to obtain the actual value, even if the device displays a fraction of CO_2.

Measuring carbon dioxide under pressure using a mainstream device has the downside of interference by both collision and pressure broadening.[5] Collision broadening is

known to affect the accuracy of capnography negatively (underestimating the result) due to the increased presence of oxygen molecules that collide with carbon dioxide molecules, causing a transfer of energy that results in broadening of the carbon dioxide absorption peak.[6,7] Pressure broadening, on the other hand, causes an overestimation of the result due to a pressure-induced shift in the absorption spectrum for carbon dioxide.[8] One study determined a measured increase in PCO_2 of 0.4 kPa per 101 kPa total pressure.[6] The results can be automatically compensated if the device has an integrated pressure and oxygen sensor. However, it requires the compensation algorithm to accept the large pressure changes commonly used inside the hyperbaric chamber versus the small atmospheric changes commonly programmed into these devices. Alternatively, mainstream capnography can be manually adjusted based on the gas mixture's oxygen content and pressure with a compensation formula/graph/table. However, it has been reported that each device works differently and would require its own compensation values.[5,8,9] One obvious advantage of sidestream capnography in this setting is that the PCO_2 is measured at normobaric pressure and the result is not influenced by collision and pressure broadening.

Mainstream and sidestream capnography have been compared extensively in the normobaric environment.[10] In the hyperbaric environment, only a few studies have been conducted. One study compared mainstream capnography with arterial blood samples and found a good correlation ($r^2 = 0.83$) but an expected large overestimation of arterial PCO_2 by the capnography of 2.22 kPa at 284 kPa treatment pressure in patients ventilated with 100% oxygen.[11] Another assessed a mainstream capnograph with various calibration gases at hyperbaric pressure and found a persistent overestimation.[5] Similarly, a recent study investigated the EMMA capnograph for use inside the hyperbaric chamber using multiple calibration gases and found consistent overestimation at 284 kPa.[12]

The EMMA capnograph is a lightweight, mobile, battery-powered (two AAA alkaline batteries) mainstream capnograph developed for pre-hospital and mobile care. The small device contains a sensor and display, providing the end-tidal carbon dioxide pressure and respiratory rate. Previous use in our hyperbaric studies has confirmed that the device functions at the highest pressures achieved in that work (557 kPa).[13] Also, oxygen breathing at 284 kPa did not cause obvious problems.[14] Those studies did not assess the accuracy of the device.

This study aimed to validate the mainstream EMMA capnograph under pressure by comparing it with sidestream capnography and, in a small convenience sample, to the gold standard arterial blood gas sampling.

Methods

TRIAL DESIGN AND PARTICIPANTS

This prospective methods comparison sub-study was part of a randomised cross-over study investigating the interaction of nitrogen and CO_2 in producing narcosis during 608 kPa exposures at the Slark Hyperbaric Unit, Te Whatu Ora Waitemata, from August to October 2022. The study protocol was approved by the Health and Disability Ethics Committee, Auckland, New Zealand (reference 16/NTA/93), and was registered with the Australian New Zealand Clinical Trial Registry (ANZCTR: U1111-1181-9722, http://www.anzctr.org.au/, RRID:SCR_002967).

Participants ($n = 12$) were healthy, certified technical divers aged between 18 and 60 years. Candidate participants currently using recreational drugs, tobacco, psychoactive medication, excessive alcohol, or over five caffeine-containing beverages a day were excluded. Prior to each hyperbaric exposure, participants had at least six hours of sleep, abstained from any caffeinated drink on the day and refrained from diving and alcohol for 24 hours prior. All twelve participants provided written informed consent, and five participants provided additional informed consent for the arterial blood gas sampling.

EXPERIMENTAL PROCEDURES

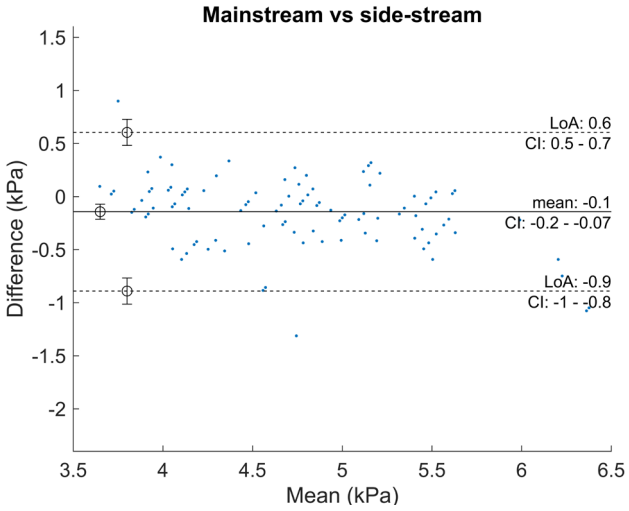
All 24 measurements (two per participant) were conducted inside a cylindrical five-person hyperbaric chamber (W.E. Smith Engineering PTY LTD, Australia). The measurements were taken at the 284 kPa stop during decompression from 608 kPa while breathing environmental air. Two hundred and eighty-four kPa was chosen as it is the most common maximum hyperbaric oxygen treatment pressure. The measurements consisted of a simultaneous analysis of $ETCO_2$ with the EMMA capnograph and sidestream capnography for five breaths through a breathing tube (Figure 1). The subjects were at rest throughout the experiment. They were instructed to seal their lips around the breathing tube and simply breathe normally for five breaths. In five participants, an additional arterial puncture during the breaths provided arterial carbon dioxide levels. In these five subjects, the breath measurements were timed to coincide with the drawing of the arterial specimen.

Mainstream EMMA capnography

Mainstream $ETCO_2$ was measured with the EMMA capnograph (Masimo, Irvine, CA, USA). Calibration was not needed according to the manufacturer's recommendations. Data points were manually transcribed.

Figure 1
Breathing tube with EMMA capnograph and sidestream sampling tube

Figure 2
Bland-Altman plot comparing the EMMA and sidestream capnograph; each breath is plotted as the mean and difference between the two measurement methods; CI – confidence interval; LoA – 95%-level of agreement



Sidestream capnography

A sampling tube was attached to the breathing tube of the EMMA capnograph. This sampling line was ported through the chamber wall, and connected to a gas analyser (ML206, ADInstruments, Dunedin, New Zealand, RRID:SCR_001620) via a t-piece to limit the gas flow to the analyser. The sampling pump was set to the maximum (approximately 200 ml·min^{-1}) to minimise the response time. Data were recorded with a PowerLab 4/25T (ADInstruments) and LabChart Pro version 8.1.24 (ADInstruments, RRID:SCR_017551) software. At the start of each measurement, calibration was performed according to the manufacturer's recommendations with a known reference gas. End-tidal carbon dioxide values were derived from the continuous carbon dioxide measurement by automated breath-by-breath detection. The $ETCO_2$ values of the five breaths were manually exported and multiplied by the environmental pressure inside the hyperbaric chamber (284 kPa).

Arterial carbon dioxide

In a convenience sample of five consenting participants, an arterial blood sample was taken. Flow in the radial and ulnar arteries was checked prior to compression using colour-flow ultrasound (Butterfly iQ, Guildford, CT, USA). The radial arterial puncture (23g needle) was performed under local anaesthesia (2% lignocaine) by an experienced anaesthetist (SJM) using palpation to locate the non-dominant radial artery. It was recorded during which of the five breaths exactly the 2 ml blood was drawn. After ensuring there was no gas in the syringe, the blood sample was depressurised and analysed directly outside the hyperbaric chamber with an iStat Alinity point-of-care blood gas analyser (Abbott, Abbott Park, IL, USA, RRID:SCR_008392).

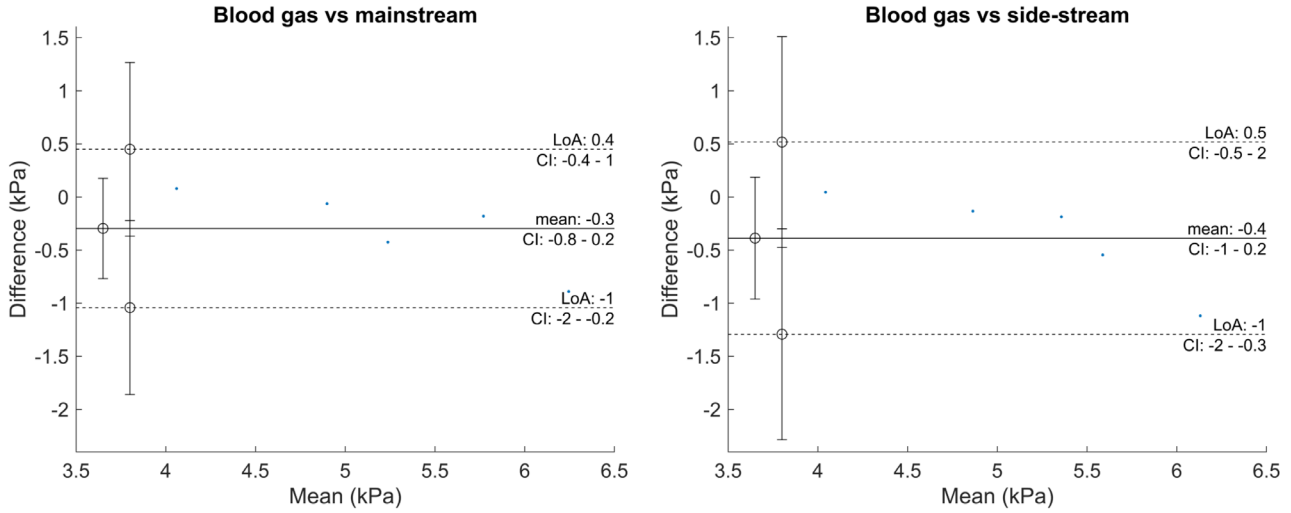
STATISTICAL ANALYSIS

All data were imported into Matlab version 2022b (Mathworks, Natick, MA, USA, RRID:SCR_001622) for analysis. The gas measurement values from all 120 breaths measured with the EMMA and sidestream capnograph datasets were presented as median and range, because of a non-normal distribution of both datasets (Kolmogorov–Smirnov test). Datasets were compared with the Wilcoxon signed rank test. Breath-by-breath end-tidal carbon dioxide values of the EMMA and sidestream capnograph were compared with a Bland-Altman analysis to determine the agreement between the two methods. We graphically presented the variation of differences between the capnography methods against their average (Bland–Altman plot).

According to the reporting standards for Bland–Altman analysis, to ensure that the 95%-limits of agreement were meaningful summary statistics of the differences, we checked the following assumptions: repeatability, constant variation, and normality.[15] Repeatability represents within-participant variation in repeated capnography measurements in the same participant. We recorded five breath measurements per participant in each of two separate pressure exposures, and assessed the repeatability of end-tidal carbon dioxide by one-way ANOVA. In contrast to the total dataset of

Figure 3

Bland-Altman plot comparing the arterial blood gas pressure and EMMA (left) or sidestream (right) capnographs; the End-tidal values in these figures are a subset of the data presented in Figure 2 (the five breaths closest to the point of arterial sampling in the five subjects who had this done); CI – confidence interval; LoA – 95%-level of agreement



120 breaths, each first, second, third, fourth and fifth breath was normally distributed (Kolmogorov-Smirnov test). We graphically checked whether the differences were normally distributed in a histogram and whether variations in the differences were constant across the range of measurements. The differences between the two measures were normally distributed (Kolmogorov-Smirnov test).

Arterial PCO_2, as the gold standard, was compared with the averaged $ETCO_2$ values of the breaths during the arterial blood gas sampling of both the EMMA and sidestream capnograph and the difference was calculated as the accuracy. The difference between the two accuracies was calculated ('accuracy difference').

In the non-inferiority comparison of accuracies of the two capnography measurements, we set *a priori* the non-inferiority margin of 0.66 kPa (5 mmHg) in accuracy difference. The size of the margin was determined from a clinical standpoint and previous reports.[16]

Results

Of the 120 breaths, 114 and 113 were captured by EMMA and sidestream capnography respectively due to recording issues with the LabChart software. The median (range) $ETCO_2$ was 4.8 (3.3–6.9) and 4.6 (3.7–5.9) kPa for the EMMA and sidestream capnographs, respectively. There was a statistically significant (but clinically insignificant) difference of about 0.1 kPa. The Bland-Altman analysis showed a 95%-level of agreement between -0.9 and 0.6 kPa (Figure 2). The visual inspection of the differences did not show skewed data, suggesting no correlation with the outcome size. The square root of the within-participant variance of $ETCO_2$ was 0.2 kPa for the EMMA capnograph and 0.1 kPa for the sidestream capnograph. One-way ANOVA showed no difference between breaths for both capnographs, indicating that repeatability was adequate. The Kolmogorov-Smirnov test of the differences showed normally distributed data.

The median (range) arterial CO_2 pressure was 5.45 (4.0–6.7) kPa, and the median $ETCO_2$ at the point of arterial sampling was 5.0 (4.1–5.8) and 5.3 (4.1–5.6) kPa for the EMMA and sidestream capnographs respectively. Compared to the arterial blood gas pressure, the non-significant difference was about 0.3 and 0.4 kPa for the EMMA and sidestream capnographs respectively (Figure 3). The *accuracy difference* between the two methods was 0.1 kPa. The number of data points was too small to analyse the levels of agreement effectively.

Discussion

In this study, we validated the use of the EMMA capnograph compared to sidestream capnography and the gold standard arterial blood gas sampling. We found a statistically significant but clinically insignificant difference between the EMMA and sidestream capnographs, with the EMMA capnograph overestimating the $ETCO_2$ by about 0.1 kPa compared to sidestream capnography. Both the EMMA and sidestream capnographs underestimated the arterial PCO_2 by about 0.3 and 0.4 kPa, respectively. The accuracy difference between these two was only 0.1 kPa, indicating agreement between the two end-tidal measurement methods. Neither was inferior, as the difference was smaller than the preselected threshold of 0.66 kPa.

The difference between the two end-tidal measurement methods and the accuracy difference were small and

clinically insignificant.[16] Even in healthy participants it is expected that $ETCO_2$ will be slightly lower than arterial PCO_2 due to alveolar dead space, i.e., gas exhaled from lung units with a high ventilation : perfusion ratio dilutes the CO_2 measured in the expired mixed alveolar gas.[17] This underestimation has been shown consistently.[18–20] Thus, the slight underestimation of the arterial PCO_2 based on $ETCO_2$ measured by either capnography method employed here was expected. In contrast, based on appraisal of previous studies, the accuracy difference was smaller than expected. The most comparable study conducted in ventilated human subjects at 284 kPa showed a much larger difference between $ETCO_2$ and arterial PCO_2 (an overestimation of 2.2 kPa).[11] We cannot explain the contrast with our results, except to observe that the subjects in that study were mechanically ventilated with 100% oxygen, and the $ETCO_2$ measurement device was different.

A pressure-broadening effect could explain the small difference found between the two capnography methods in the present study. The increased pressure inside the hyperbaric chamber, to which the EMMA capnograph was exposed, could have caused an overestimation of the $ETCO_2$ value. This effect is consistent so that the difference can be anticipated, as shown by others as a linear relationship between pressure and the results from the EMMA capnograph.[12]

STRENGTHS AND LIMITATIONS

A limitation of the EMMA capnograph was the inability to be calibrated with a reference gas, which may have contributed to the slight difference between the two capnography measures. Nevertheless, this head-to-head comparison between the EMMA capnograph and a research-grade sidestream capnograph suggested that this small, portable and battery-powered device performs well under the circumstances of our experiment. We undertook two measurements of five breaths with twelve participants allowing us to compare 113 data points. A limitation is that we collected only five arterial blood gas samples due to the complexity of taking blood gas samples inside the hyperbaric chamber. This could have been increased by increasing the number of participants or by taking multiple blood samples via a catheter from the same five participants. The number of data points was too small to analyse the levels of agreement effectively. However, the collected data showed good agreement between both capnographs and the arterial blood sampling.

We measured the PCO_2 in end-tidal breaths at the point the arterial blood gas sample was taken. Previous research has shown a short (approximately 15 second – approximately three breath) delay between peripheral arterial PO_2 and end-tidal O_2 due to the time it takes for blood to flow from the lungs to the puncture site.[21] It seems likely that the potential for error to be introduced due to this delay is minimal in our measurements because our participants were resting in a steady state.

In previous research to 608 kPa,[13] we noted that the EMMA capnograph produced errors over 557 kPa, but sidestream capnography would be a viable option for such higher pressure exposures. Nowadays, pressures beyond 284 kPa are very rarely used in hyperbaric treatments. Based on our data, at the pressures at which most hyperbaric treatments are conducted, the EMMA capnograph provides $ETCO_2$ measurements that are sufficiently accurate for decision-making during ventilation of an intubated patient. One caveat is that our subjects were breathing chamber air and not oxygen. Oxygen breathing can cause an increase in alveolar dead space[22] which would increase the difference between $ETCO_2$ (measured by either mainstream or side stream methods) and the true arterial PCO_2, and hyperoxic breathing may also affect collision broadening.[5] In future work, this study can be repeated with oxygen breathing, preferably in ventilated patients.

Conclusion

This study showed that the EMMA capnograph slightly overestimated the $ETCO_2$ and slightly underestimated the arterial PCO_2 in human subjects spontaneously breathing air in a hyperbaric environment at 284 kPa. The inaccuracies were clinically insignificant and if these findings were replicable in patients ventilated with 100% oxygen, they would establish the EMMA capnograph as suitable for monitoring ventilated patients during hyperbaric oxygen treatment.

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Conflicts of interest and funding

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