

Partial pressure of end-tidal CO₂ sampled via an intranasal catheter as a substitute for partial pressure of arterial CO₂ in dogs

D. Pang, BVSc, J. Hethey, N. A. Caulkett, DVM, MVetSc, DACVA and T. Duke, BVetMed, DVA, DACVA, DECVA

Abstract

Objective: To demonstrate correlation and clinical usefulness of the partial pressure of end-tidal CO₂ (ETCO₂) measurement by nasal catheter placement in sedated dogs with and without concurrent nasal oxygen administration as a substitute for partial pressure of arterial CO₂ (PaCO₂).

Design: Prospective, cross-over trial.

Setting: University of Saskatchewan veterinary research laboratory.

Animals: Six cross-breed dogs with a mean (\pm SD) weight of 29.1 \pm 4.03 kg.

Interventions: All dogs were sedated with 5 μ g/kg medetomidine intravenously (IV) and an arterial catheter was placed in a dorsal pedal artery for removal of blood for gas analysis. A nasal catheter was placed in the ventral meatus and connected to a capnometer for ETCO₂ measurements in all dogs. Dogs receiving supplemental nasal oxygen had a second nasal catheter placed in the contralateral naris.

Measurements and main results: In the group without nasal oxygen supplementation, the ETCO₂ measurement underestimated (negative bias) the PaCO₂ by -2.20 mmHg with limits of agreement (95% confidence interval) of $-5.79, 1.39$ mmHg. In the group receiving oxygen supplementation, ETCO₂ measurement underestimated (negative bias) the PaCO₂ by -2.46 mmHg with limits of agreement (95% confidence interval) of $-8.42, 3.50$ mmHg.

Conclusions: The results of this study demonstrate that ETCO₂ monitoring via a nasal catheter provides a clinically acceptable substitute to arterial blood gas analysis as a means of monitoring ventilation in healthy, sedated dogs. The limits of agreement were within acceptable limits with and without concurrent insufflation of oxygen.

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Keywords: ETCO₂, expired carbon dioxide, nasal catheter, nasal oxygen

Introduction

Monitoring end-tidal CO₂ partial pressure (ETCO₂) using a capnometer is accepted as an indirect approximation of arterial CO₂ partial pressure (PaCO₂).^{1–3} Capnometry is included as one of the basic standards of monitoring adequate ventilation during general anesthesia according to the American Society of Anesthesiologists.^{4,5} When endotracheal intubation is used,

ETCO₂ is easily measured by attaching the sampling line of a capnometer to the distal end of the endotracheal tube (sidestream capnometry). However, due to the presence of underlying respiratory or neuromuscular disease, or due to the use of sedative drugs, many extubated veterinary patients in the perioperative phase and critical patients in the intensive care unit may benefit from continuous monitoring of ventilation. The only means of accurately monitoring the adequacy of ventilation in this group of patients is arterial blood gas analysis, which requires arterial puncture or catheter placement. Although arterial blood gas analysis is accepted as the gold standard in the assessment of ventilation, sample collection can be technically challenging to perform and access to arterial sites may be limited due to patient size or bandaging.⁶ Furthermore,

From the Department of Clinical Sciences, Faculté de médecine vétérinaire, Université de Montréal, Québec, Canada (Pang), and the Department of Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, Canada (Hethey, Caulkett, Duke).

Address correspondence and reprint requests to:

Dr. Tanya Duke, Department Small Animal Clinical Sciences, Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Dr., Saskatoon, SK, Canada, S7N 5B4.
E-mail: tanya.duke@usask.ca

complications associated with arterial blood sampling include transient or permanent artery occlusion, bleeding, hematoma, infection, and patient discomfort.⁷

Pulse oximetry is useful for detection of hypoxemia, but this technique does not monitor CO₂ status and therefore will not provide an early indicator of hypoventilation, particularly in patients administered supplemental oxygen. A potential alternative to arterial blood gas sampling and pulse oximetry to monitor adequate ventilation in non-intubated patients is to use ETCO₂ measurements sampled through an intra-nasal catheter. Nasal catheters are used in dogs for delivery of oxygen and have been demonstrated to be highly effective at increasing the fraction of inspired oxygen (FIO₂). A flow rate of oxygen of >100 mL/kg/min is associated with an FIO₂ of >40%.^{8,9} The use of nasal catheters to monitor ETCO₂ has been previously documented in children and adults and has also been investigated in dogs and cats.^{10,11} The previously reported study in dogs and cats documented the accuracy of ETCO₂ monitoring using cannulae placed at the level of the nares.¹¹ The authors in that study found that panting in dogs decreased instrument accuracy. That study, however, was not designed to investigate the use of longer intra-nasal catheters with concurrent administration of oxygen. The objectives of this prospective study were to demonstrate correlation and clinical usefulness of ETCO₂ measurement using long intra-nasal catheters in healthy, sedated dogs with and without concurrent nasal oxygen administration as a substitute for taking arterial blood samples to measure PaCO₂.

Material and Methods

This study was approved by the University of Saskatchewan Animal Care Protocol Review Committee, and animals were kept according to Canadian Council for Animal Care guidelines. Six, young-adult, Husky-cross dogs weighing a mean (\pm SD) of 29.1 (\pm 4.03) kg were used in the study. All dogs were healthy according to physical, hematological, and serum biochemical examinations. Food was withheld for 12 hours before the study.

Before use in each dog, the side-stream capnometer^a was calibrated using a known concentration of gases, and the oxygen flowmeter was calibrated using a Wright's respirometer. The capnometer was programmed to sample gases at a withdrawal rate of 50 mL/min.

The study was conducted as a prospective, cross-over trial with a rest phase of 1 week between each trial period. Dogs were randomly divided into 2 groups. The first group (Group 1) underwent ETCO₂ recordings without concurrent oxygen insufflation, and the second group (Group 2) underwent ETCO₂ recordings while oxygen was insufflated (150 mL/kg/min) through a

second nasal catheter in the contralateral ventral meatus. In both study groups, each dog was sedated with 5 μ g/kg medetomidine^b administered intravenously (IV) in order to provide different partial pressures of arterial CO₂ through central respiratory center depressant effects. Medetomidine was chosen to produce deliberate hypoventilation based on a pilot study using various sedation techniques. Following sedation, the area of skin overlying the dorsal pedal artery was aseptically prepared for placement of an over-the-needle catheter (22 G).^c The catheter was connected via a short length of extension tubing to a 3-way stopcock to allow anaerobic withdrawal of arterial blood samples.

A 5 Fr feeding tube^d was used as a nasal catheter and positioned in the ventral meatus of the nasal cavity. The catheter was premeasured from the level of the nostril to the lateral canthus of the eye and marked proximally with a black line. Topical local anesthetic solution^e was instilled into the nasal cavity, and the nasal catheter was lubricated with local anesthetic gel.^f The nasal catheter was advanced until the black mark was level with the nostril. The nasal catheter was glued at the site of exit from the nostril (alar cartilage) and at the craniodorsal area of the head. The proximal end of the nasal catheter was attached to the capnometer via the instrument's sampling line. For dogs receiving concurrent O₂ nasal insufflation, the same procedure was used to place another catheter in the contralateral nasal meatus to the level of the medial canthus of the eye, and O₂ was delivered through this second catheter at a flow rate of 150 mL/kg/min.⁹

Animals were lightly restrained in lateral recumbency for the procedure except following complete medetomidine reversal when they were allowed to return to sternal recumbency.

Following instrumentation, 7–8 arterial samples were withdrawn from each dog using purpose-specific, heparinized syringes^g and stored on ice. Samples were analyzed^h within 1 hour of collection and results were corrected to the rectal temperature of the dog. Blood samples were taken during full sedation, partial sedation (after 12.5 μ g/kg atipamezoleⁱ IV), and after full recovery from sedation (following a further 12.5 μ g/kg atipamezole IV). During the period in which the arterial sample was withdrawn (approximately 10 seconds), average ETCO₂ concentration and respiratory rates were calculated. The mean ETCO₂ was used for subsequent data analysis. Following the end of each study period, all catheters were removed and the dog was supervised until full recovery from sedation.

Statistical analyses

Data from paired samples were subjected to linear regression analysis and the Bland and Altman method for

Table 1: Bias, precision, limits of agreement, and correlation coefficient (*r*) for Group 1 (no oxygen insufflation) and Group 2 (concurrent oxygen insufflation) comparing accuracy of using intranasal CO₂ measurements in place of PaCO₂

	<i>n</i>	$y = bx + a$	<i>r</i>	Bias (mmHg)	Precision (SD; mmHg)	Limits of agreement (95% CI) (1.96SD; mmHg)
Group 1 (no nasal O ₂)	44	$b = 0.95$ $a = -0.33$	0.88	-2.20	1.83	-5.79, 1.39
Group 2 (nasal oxygen)	35	$b = 1.05$ $a = -4.19$	0.80	-2.46	3.04	-8.42, 3.50

The regression equation is defined by $y = bx + a$, where *a* is the intercept and *b* is the slope giving the amount of change in *y* for one unit change in *x*. *n*, number of paired data.

assessment of suitability of 2 methods of clinical measurement.¹² A modification of the original Bland and Altman method was used.^{13,14} In the original method, bias is calculated as the 'gold standard' minus the 'new method'.¹² For this study, bias was calculated as the 'new method' (capnometry measurement) minus the 'gold standard' (arterial blood gas measurement) method. This approach provides a more intuitive method of presenting the bias where an underestimation of the 'gold standard' method by the 'new method' is presented as a negative figure. Where appropriate, data analyses were performed with statistical software programs.^{j,k} The level of significance was set at $P < 0.05$.

Results

Table 1 summarizes the results of both groups. Of 48 paired (ETCO₂ and arterial blood gas measurements) samples for Group 1, 4 were excluded from statistical analyses. Two of these exclusions were due to technical difficulties with the blood gas analyzer. The other 2 excluded samples were from the same animal and were

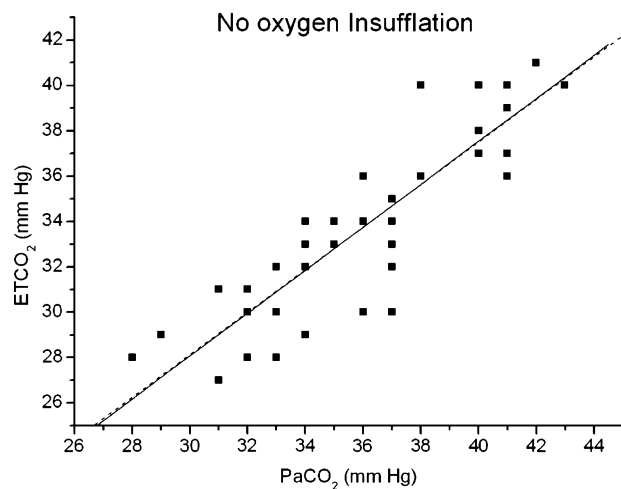


Figure 1: Scatterplot of partial pressure of arterial CO₂ (PaCO₂) against partial pressure of end-tidal CO₂ (ETCO₂). Regression line (solid line) and line of unity (dashed line) overlies one another.

not included due to lack of normal alveolar plateau generation on the capnograph as a result of snorting or sneezing that resulted in extremely low ETCO₂ values (16 and 24 mmHg). In Group 1, good linear correlation ($r = 0.88$) existed between PaCO₂ and ETCO₂ (Figure 1). The bias and limits of agreement for Group 1 reflect a consistent underestimation of PaCO₂ by nasal ETCO₂ (-2.20 mmHg) within narrow limits of agreement (-2.20 ± 1.96 SD; $[-5.79, 1.39]$). A Bland–Altman plot (Figure 2) illustrates this relationship.

From Group 2, 35 paired samples were included in the analyses. Four samples were excluded (3 from the same dog) due to lack of a normal alveolar plateau on the capnograph as a result of snorting following partial or full reversal of medetomidine. The data from 1 dog (7 paired samples) were excluded from the analyses due to difficulties in instrumentation that resulted in further sedation with medetomidine.

The bias for Group 2 reflects a consistent underestimation of PaCO₂ by nasal ETCO₂ (-2.46 mmHg) similar to Group 1. The limits of agreement for Group 2 (-2.46 ± 1.96 SD; $[-8.42, 3.50]$) are wider than those of Group 1. These relationships are illustrated in Figures 3 and 4.

Discussion

Since the early descriptions of ETCO₂ measurement through nasal cannulae, the technique has been shown to be comparable with PaCO₂ in both adults and children.^{1,10,15–19} The previous study in cats and dogs using cannulae positioned at the level of the nares also demonstrated acceptable accuracy.¹¹ In non-panting, healthy dogs, the linear correlation between ETCO₂ and PaCO₂ was 0.84 and the 95% confidence interval of the difference was ± 3.2 mmHg. This finding is similar to the results of the current study. The 2 studies also found that correlation was poor when the dog was panting. Because of poor correlation (underestimation of PaCO₂) during this study, data were excluded from any dog exhibiting panting or other abnormal breathing patterns resulting in a poorly defined alveolar plateau.

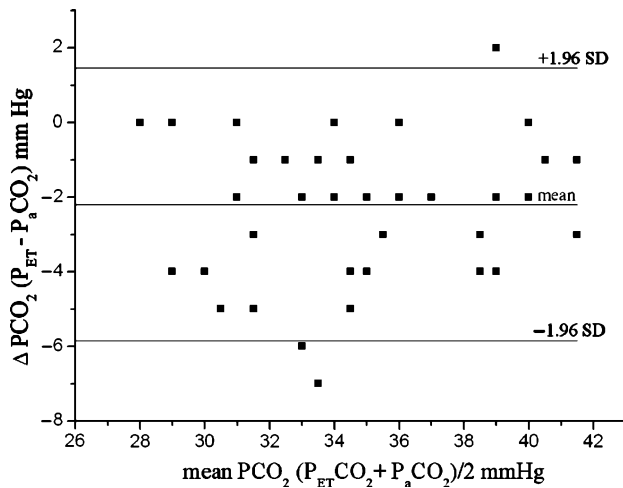


Figure 2: Bland–Altman plot for Group 1 illustrating the difference in partial pressure of CO₂ (ETCO₂ – PaCO₂; mmHg) plotted against the mean of ETCO₂+PaCO₂ (mmHg). Limits of agreement are illustrated by lines (± 1.96 SD). There are fewer number of points illustrated than analyzed due to replication of points.

Without concurrent oxygen insufflation, ETCO₂ measured via a nasal catheter demonstrated a negative bias of –2.20 mmHg, a figure small enough to be clinically insignificant. However, in order to put the usefulness of this technique into context, the limits of agreement must be taken into account. As described by Bland and

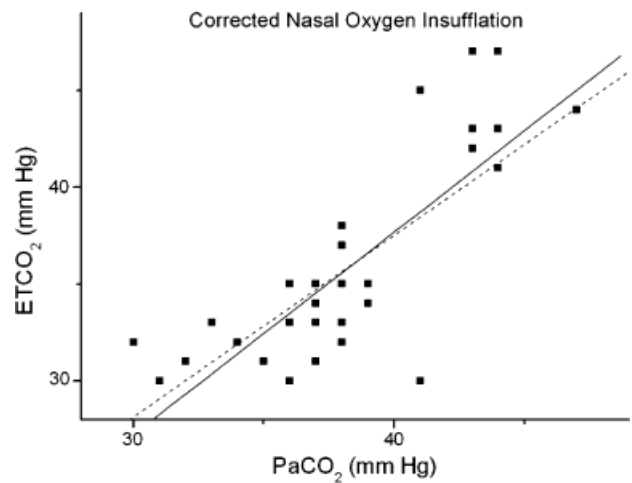


Figure 3: Scatterplot of partial pressure of arterial CO₂ (PaCO₂) against partial pressure of end-tidal CO₂ (ETCO₂). Regression line (solid line) and line of unity (dashed line) are shown.

Altman, provided the limits of agreement lie within a clinically acceptable range, a new technique (i.e., ETCO₂ by nasal catheter) can be used as a substitute for the gold standard technique (i.e., PaCO₂ by arterial blood gas analysis).¹² The results of this study demonstrate a clinically acceptable degree of precision (± 1.96 SD, or ± 3.59 mmHg) very similar to the previous study with the limits of agreement lying within a clinically acceptable range (– 5.79 to 1.39 mmHg). The pre-

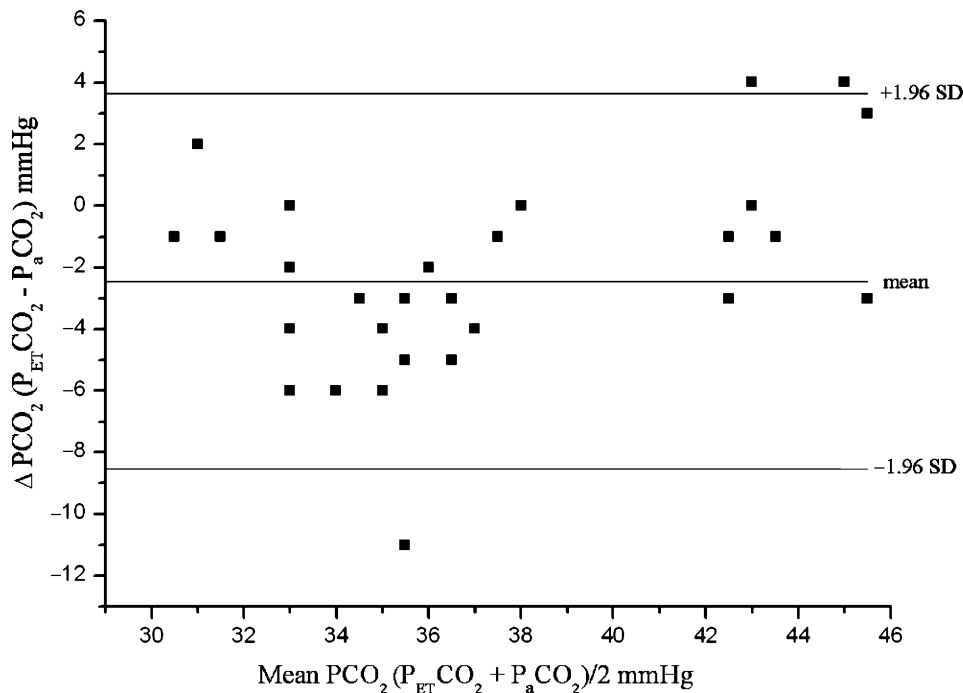


Figure 4: Bland–Altman plot for Group 2 illustrating the difference in partial pressure of CO₂ (ETCO₂ – PaCO₂; mmHg) plotted against the mean of ETCO₂+PaCO₂ (mmHg). Limits of agreement are illustrated by lines (± 1.96 SD). There are fewer number of points illustrated than analyzed due to replication of points.

vious study also found that the ETCO₂ tended to slightly underestimate the PaCO₂.¹¹ The use of concurrent oxygen insufflation via the contralateral nasal chamber also resulted in a small underestimation (−2.46 mmHg) of PaCO₂. The degree of precision (± 1.96 SD, or ± 5.96 mmHg) was lower and therefore the limits of agreement were wider (−8.42–3.50 mmHg). This lesser degree of precision is also within clinically acceptable limits.

Sampling error has been reported as a cause of the difference between ETCO₂ and PaCO₂ with and without concurrent insufflation of oxygen.^{17,19} Sampling errors occur as a result of line blockage or dilution of the ETCO₂ sample by ambient air or fresh gas flow. These errors may also be caused by mouth breathing, hypoventilation, low tidal volumes, or dilution of the ETCO₂ sample by close proximity of concurrent oxygen insufflation.^{17,19} Neither line blockage nor mouth breathing were observed during the study period, although secretions tended to enter the sampling line more often compared with conventional sampling from an endotracheal tube. Based on study design, it is difficult to completely rule out intended hypoventilation or low tidal volume as causes of sample dilution, though arterial blood gas analysis did not reveal severe hypoventilation and medetomidine has not been shown to greatly decrease tidal volume in dogs.²⁰ This study found that medetomidine produced a breathing pattern most likely to provide a reasonable alveolar plateau.

Neither oral examination nor radiography was undertaken to verify relative catheter positions and it is possible that the tips of both catheters were close to one another due to the proximity of insertion levels (medial and lateral canthi). The likely proximity of catheter tips may have resulted in the wider limits of agreement in the presence of concurrent oxygen insufflation.

In order to offset the effect of sample dilution by concurrent oxygen insufflation, the sampling flow rate of the capnometer was set to 50 mL/min. Although not investigated, the use of lower sampling flow rates available with microstream capnography may improve accuracy further and it is possible that the use of higher sampling rates, in the range of 150–200 mL/min employed by most conventional sidestream capnometers, could result in a further decrease in accuracy due to entrainment of insufflated oxygen or ambient air.¹⁰

Further improvements in precision during concurrent administration of oxygen may also be possible by adjusting catheter position or using nasal cannulae in place of nasal catheters. The exact positioning of nasal catheters in the pharyngeal region does not appear to affect the ETCO₂, and the relative positioning of the sample and insufflation catheters has a greater effect on the accuracy of ETCO₂ measurements.¹⁶ In a study of 9 healthy hu-

man volunteers, comparisons of 3 different pharyngeal catheter positions did not affect ETCO₂ measurements.¹⁶ However, the oxygen insufflation catheter was located nasally; this difference in location between sampling and administration catheters is likely to improve precision further as oxygen insufflation and ETCO₂ sampling via the same naris significantly increases bias and decreases correlation.¹⁷ Furthermore, delivery of oxygen through 1 prong of a nasal cannula and ETCO₂ sampling through the other was not found to affect ETCO₂ measurements.¹⁷

The findings of this study agree with those from studies performed in healthy, adult human patients and heterogeneous pediatric populations without severe pulmonary or cardiac disease.^{15,16} The results of this study also concur with those from the other veterinary study in which nasal cannulae were used in healthy, non-panting dogs.¹¹ The effect of severe pulmonary or cardiac disease is less clear. Friesen and Alswang,¹⁷ in a study of 97 pediatric patients, documented the effects of various conditions on correlation and bias. Mouth breathing, oxygen insufflation through the ipsilateral naris, and cyanotic heart disease were found to significantly increase the bias and decrease correlation. Of these factors, mouth breathing and oxygen insufflation through the ipsilateral naris increased bias to a greater degree than cyanotic heart disease. Unfortunately, limits of agreement were not calculated.

From the results of this study, it can be concluded that ETCO₂ monitoring via 'pharyngeal' placement of a nasal catheter provides a clinically acceptable substitute to multiple arterial blood gas analyses as a means of monitoring ventilation in healthy dogs with non-panting, normal breathing patterns. The degree of precision and limits of agreement were within acceptable limits with and without concurrent insufflation of oxygen. However, attention must be paid to potential sampling errors and results interpreted in light of the clinical status of the patient. Evaluation of the capnograph waveform is recommended as an adjunct to assessing the reliability of results since failure to generate an alveolar plateau (phase III) resulted in aberrant ETCO₂ measurements. The effects of sedation with drugs other than medetomidine on the accuracy of this technique cannot be predicted from the results of this study. Refinements to this technique by altering the site of sampling catheter placement and ensuring separation of sampling and oxygen insufflation lines may reduce the degree of difference between ETCO₂ and PaCO₂ further.

Footnotes

- ^a POET IQ Gas Analyzer, Criticare Systems Inc., Waukesha, WI.
- ^b Medetomidine hydrochloride, Novartis Animal Health Canada Inc., Mississauga, ON, Canada.
- ^c Insite-W, Becton Dickinson, Infusion Therapy Systems Inc., Sandy, UT.

- ^d MED-RX 5Fr 15" Feeding Tube, Benlan Inc., Oakville, ON, Canada.
^e Alcaine ophthalmic solution, Alcon Canada Inc., Mississauga, ON, Canada.
^f Xylocaine 2% Jelly. Astra Pharm Inc., Mississauga, ON, Canada.
^g PICO™ 50 arterial blood sampler, Radiometer Medical A/S, Copenhagen, Denmark.
^h Radiometer ABL 5 Blood Gas Analyzer, Copenhagen, Denmark.
ⁱ Atipamezole hydrochloride, Novartis Animal Health Canada Inc., Mississauga, ON, Canada.
^j OriginPro 7.5, OriginLab Corporation, Northampton, MA.
^k SPSS 11.0.2, Copyright © 2004, SPSS Inc., Chicago, IL.

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