Suitability of lingual venous blood to determine the acid-base and blood gas status of dogs under anesthesia

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Running title: lingual blood gas analysis in dogs

Abstract

Objective To assess the suitability of lingual venous blood (LBG) samples as a substitute for arterial blood (ABG) samples in determining acid-base balance and blood gas status in clinical cases anesthetized for elective procedures and during medetomidine and isoflurane administration under experimental conditions.

Study design Prospective, randomized clinical and experimental study.

Animals Clinical population of 18 ASA I/II dogs for elective surgery and 5 healthy Beagles for experimental study.

Methods Blood sampling was simultaneously performed at dorsal pedal arterial and lingual venous sites, generating paired data. Two paired samples were collected from each dog in the clinical arm and four from each dog in the experimental arm (two during isoflurane anesthesia and two during isoflurane plus medetomidine). A modified Bland and Altman method was used to examine data from the clinical arm and the experimental data were subjected to a paired Sign's Test following transformation where appropriate.

Results The pH of LBG overestimated ABG, with limits of agreement of (-0.01, 0.02). The PCO_2 of LBG overestimated ABG by 0.6 mmHg [0.1 kPa], with limits of agreement of (-3.5, 4.6) mmHg [-0.5, 0.6 kPa]. The PO_2 of LBG underestimated ABG by 86.3 mmHg [-11.5 kPa], with limits of agreement of (-199.8, 27.3) mmHg [-26.6, 3.6 kPa]. During medetomidine

administration values for PO_2 ($p = 0.03$) and lactate ($p = 0.03$) were lower for LBG when compared with ABG. The LBG value of PO_2 was lower ($p = 0.03$) during medetomidine and isoflurane administration versus isoflurane alone.

Conclusions and clinical relevance The pH and PCO_2 of LBG samples provide clinically acceptable substitutes of ABG samples in the patient population studied. The wider limits of agreement for PO_2 render it less reliable as a substitute for ABG. The difference in PO_2 identified between LBG and ABG during medetomidine administration may not preclude the use of LBG samples as substitutes for ABG samples.

Keywords: anesthesia, medetomidine, lingual, arterial, blood gas, dog

Introduction

Arterial blood (ABG) sample analysis provides critical information in the monitoring of blood gas and acid-base homeostasis (Wagner et al. 1991). However, sampling of arterial blood is not without complications. These include bleeding, transient or permanent vessel obstruction, infection and patient discomfort (Mortensen 1967; Shapiro et al. 1994). Furthermore, the small size of many animals makes arterial puncture or the placement of catheters difficult and sites may be rendered inaccessible during surgery (van Sluijs et al. 1983; Wagner et al. 1991).

Alternative techniques to arterial sampling have been investigated in both humans (Lundsgaard & Moller 1922; Singer et al. 1955; Maas & van Heijst 1961; Langlands & Wallace 1965; Harrison et al. 1997; Yildizdas et al. 2004) and animals (Sharpe et al. 1968; Rodkey et al. 1978; van Sluijs et al. 1983; Abou-Madi & Robertson 1988; Wagner et al. 1991).
Sites investigated have included capillary blood samples (CBG) in humans from the finger or heel (Harrison et al. 1997; Escalante-Kanashiro & Tantalean-Da-Fieno 2000; Yildizdas et al. 2004) and earlobe (Dar et al. 1995; Sauty et al. 1996; Eaton et al. 2001). In dogs, the margin of the ear (Rodkey et al. 1978; van Sluijs et al. 1983) and lingual venous samples (Abou-Madi & Robertson 1988; Wagner et al. 1991) have been used for sample collection. The theory underlying CBG and lingual venous blood (LBG) samples is that a small arterio-venous difference in parameters of interest (partial pressure of oxygen, PO_2; partial pressure of carbon dioxide, PCO_2; standard base excess; SBE, pH and lactate) allows substitution of these sample sites for ABG. Compared with ABG, these sites are less challenging to sample and associated with fewer complications (Abou-Madi & Robertson 1988; Wagner et al. 1991; Dar et al. 1995).

It may be a misnomer to refer to CBG sites as "capillary" as typical sampling sites probably reflect a mixture of capillary, arteriolar and venular blood. The precise composition of the blood likely varies with the degree of local perfusion and vasoconstriction (Pandit 1995).

This study comprised two parts. The aim of the clinical arm was to quantify the relationship between arterial and lingual venous blood samples in anesthetized dogs for selected parameters commonly employed in the assessment of respiratory function and acid-base homeostasis. The aim of the experimental arm was a pilot study to provide initial information on the potential effect of a constant rate infusion (CRI) of medetomidine during isoflurane anesthesia on the same parameters using the same sampling sites.

Material and methods

This study was approved by the Animal Use and Ethics Committee of the Université de Montréal.

For the clinical arm, dogs scheduled for orthopedic or soft tissue surgery at the Université de Montréal small animal hospital. Inclusion criteria included ASA class I/II patients of the small animal clinic, scheduled to have an arterial catheter placed for direct systemic blood pressure monitoring, and arterial blood sampling, as part of anesthetic management. Exclusion criteria included known coagulopathies, dental disease and skin disease at the site of arterial catheter placement. Samples were only taken when the following criteria were met: direct mean systemic arterial blood pressure (MAP) of 60-100 mmHg, esophageal temperature of 37.0 ± 1°C, and normocapnea (partial pressure of end-tidal carbon dioxide [$P_{E'}CO_2$] between 35-45 mmHg (4.7 – 6.0 kPa).

No exclusion was made on the basis of breed, weight (median [range] 27.5 [4.6 – 60] kg) or age (median [range] 50 [3 – 149] months). Breeds included were, Australian Shepherd (2), mixed breed (4), Bouvier de Flandres (1), Chesapeake Bay Retriever (1), Leonberger (1), Bull Mastiff (1), Pyrenean Mountain Dog (1), Labrador Retriever (2), Airedale (1), Shih Tzu (1), Rottweiler (1), Golden Retriever (1), Shetland Sheepdog (1). Two paired samples, each pair comprising an LBG and ABG, were taken from each animal and with a minimum period of 20 minutes between samples. Immediately prior to sample collection, the following physiological parameters were recorded: heart rate (as calculated from the arterial pressure trace; HR), MAP, esophageal temperature (Temperature Probe, Esophageal/Rectal, 700 Series, Adult Reusable, Datascope Corporation, Montvale, NJ, USA) and P_ECO_2 (NPB-75, Nellcor Puritan Bennett, Plesanton, CA, USA). Body temperature was monitored using an esophageal probe inserted to the level of the fifth intercostal space. Sampling was not performed when physiologic parameters were outside the predetermined ranges. A catheter (20-SWG, 1.16 inch or 22-SWG, 1.00 inch, BD Insyte-W, Becton Dickinson Infusion Therapy Systems Inc, Sandy, Utah, USA) to allow monitoring of systemic arterial blood pressure and repeated sampling was introduced into either the left or right dorsal pedal artery, flushed with heparinized saline and connected to a display unit (Datascope 2000, Datascope Corporation, Montvale, NJ, USA) via an extension tubing pre-filled with heparinized saline and a transducer (TruWave Disposable Pressure Transducer, Edwards Lifesciences LLC, Irvine, CA, USA). A 3-way stopcock close to the catheter allowed anaerobic withdrawal of arterial blood samples. Sampling was performed simultaneously, and all lingual venous samples were taken by one of two experienced anesthesia technicians. The LBG samples were taken from the smallest possible vessel using a 25-SWG 1 inch needle attached to

a pre-heparinized 1 mL plastic syringe. Syringes were pre-heparinized with 1000 UmL^{-1} Lithium heparin by filling each syringe completely with heparin, then returning the heparin to the bottle and expelling as much heparin as possible from the syringe. This was achieved by filling each syringe with air before forcibly expelling it. This was repeated 2 – 3 times. Whenever possible, the syringe was filled completely with blood. Arterial blood sampling and analysis were performed using a standardized technique. Briefly, the three-way stopcock attached to the arterial catheter was opened and blood allowed to flow freely for 5 seconds, at which point a pre-heparinized 1 mL syringe was attached and an anaerobic arterial blood sample withdrawn. Following sampling, the arterial catheter was immediately flushed and any air bubbles present were evacuated from the syringe. The syringe was then capped. Samples were analyzed (StatProfile M, Nova Biomedical, Waltham, MA, USA) within 5 minutes of collection and the order of analysis randomized (www.random.org). Sample analysis was corrected for oesophageal temperature.

The capnograph used was within one year of manufacture, during which time calibration is not required, as per the manufacturer's recommendations. The blood gas analyzer performed an autocalibration prior to sample collection and every four hours throughout the day.

A total of 22 animals were recruited for the study. Of these, 3 were subsequently excluded due to a physical status that did not meet the inclusion criteria, and data from one animal were lost. Therefore 18 animals, from which 2 paired samples were taken from each, were included in the statistical analysis.

For the experimental arm, the animals investigated were part of another study for which general anesthesia and arterial catheter placement was required. Animal Use and Ethics

148 Committee approval was granted for this study. Five Beagle dogs underwent arterial catheter
149 instrumentation and blood sampling as described above following induction of anesthesia using
150 isoflurane in oxygen delivered by face-mask. No premedication was given and ventilation was
151 controlled with a tidal volume of 15 mL kg^{-1} $minute^{-1}$ and respiratory rate adjusted to maintain a
152 $P_{E'}CO_2$ between 35 – 45 mmHg (4.7 – 6.0 kPa). Additionally, a 20-SWG, 1.88 inch catheter was
153 placed in either the left or right jugular vein to allow jugular venous blood (VBG) samples to be
154 drawn simultaneously with arterial and lingual venous samples. The median [range] weight and
155 age were 12 [9.8 – 12.4] kg and 16.2 [20 – 43] months, respectively. Each dog received a loading
156 dose and constant rate infusion (CRI) of medetomidine whilst under general anesthesia, induced
157 and maintained with isoflurane (constant $F_{E'}$iso% of 1.3). One hour of general anesthesia
158 maintained with isoflurane alone preceded one hour of medetomidine administration in addition
159 to isoflurane. Four paired samples were taken from each animal; two during isoflurane anesthesia
160 and two during the medetomidine CRI plus isoflurane anesthesia. Each dog received a loading
161 dose of 4 μg kg^{-1} followed by a CRI of 4 μg kg^{-1} $hour^{-1}$.

162 ***Statistical analyses***

163 Data from the clinical arm were analyzed using a modification of the method described by Bland
164 and Altman to assess agreement between two methods of clinical measurement (Caulkett et al.
165 1998). In the original method, bias was calculated as the "gold standard" minus the "new
166 method" (Bland & Altman 1986). For this study, bias was calculated as the "new method" (LBG)
167 minus the "gold standard" (ABG) method. This provides a more intuitive method of presenting
168 the bias, where an underestimation of the "gold standard" method by the "new method" is
169 presented as a negative figure. Data analyses were performed with statistical software programs

(Origin Pro version 7.5, OriginLab Corp., Northhampton, MA, USA and MedCalc version 8.1.1, MedCalc Software, Mariakerke, Belgium). The following parameters were subjected to analysis: pH, PO_2, PCO_2, standard base excess (SBE) and lactate. Bias was defined as the mean value of the difference between LBG and ABG. Limits of agreement were defined as 1.96 standard deviations (SD) of the bias. Data from the experimental arm were not subjected to Bland and Altman analysis due to the small number of animals. The parameters evaluated were pH, PO_2, PCO_2 and lactate. Prior to the analysis of paired samples with/without medetomidine, data were transformed when necessary as follows: arcsine transformation for PO_2, logarithmic transformation for PCO_2 and lactate. Data were then subjected to a paired Sign's test. Results were considered significant if $p < 0.05$.

Results

The results from the clinical arm are summarized for each parameter subjected to analysis in Table 1. For pH, a small overestimation of ABG by LBG with narrow limits of agreement (-0.01, 0.02) was present (Figure 1). The LBG sample systematically underestimated the ABG sample for PO_2 (-86.3 mmHg, [-11.5 kPa]) with limits of agreement ranging from -199.8 to 27.3 mmHg [-26.6 to 3.6 kPa] (Figure 2). The median [range] of ABG PO_2 sampled was 507.0 [401.3 – 568.5] mmHg. In contrast, LBG PCO_2 samples overestimated ABG (0.6 mmHg [0.1 kPa]) with limits of agreement from -3.5 to 4.6 mmHg [-0.5 to 0.6 kPa] (Figure 3). The SBE of the LBG sample overestimated ABG (0.6 mmol L^{-1}) with limits of agreement of -1.2 to 2.3 mmol L^{-1}. Similarly to pH, lactate in the LBG sample overestimated that in the ABG sample by a small amount with narrow limits of agreement (-0.3, 0.3 mmol L^{-1}).

The results of the experimental arm are presented in Table 2. For pH, a significant difference existed between LBG and VBG ($p = 0.03$), and between ABG and VBG ($p = 0.01$) during both isoflurane administration alone and in combination with medetomidine (identical p values). Comparing treatment groups resulted in a significantly higher pH ($p = 0.01$) in the VBG samples during isoflurane alone compared to pH values during medetomidine plus isoflurane. Analysis of PO_2 values demonstrated a significantly greater PO_2 from LBG compared with VBG ($p = 0.03$) and from ABG compared with VBG ($p = 0.008$) during both isoflurane administration alone and in combination with medetomidine. A significantly lower PO_2 was present in LBG compared with ABG ($p = 0.03$) during both isoflurane administration alone and in combination with medetomidine. A comparison of treatment groups demonstrated a significantly lower PO_2 in the VBG ($p = 0.008$) and LBG ($p = 0.03$) samples during medetomidine administration. Analyses of PCO_2 values demonstrated significantly lower values for both LBG samples when compared with VBG ($p = 0.03$), and ABG samples when compared with VBG ($p = 0.008$) during each treatment. There was no significant difference between LBG and ABG sampling sites for each treatment. Comparing treatments demonstrated a significantly lower PCO_{2}. ($p = 0.008$) in the VBG samples during isoflurane administration alone. A comparison between sampling sites and treatment groups demonstrated a significant difference for lactate only when comparing LBG values with and without medetomidine administration. Medetomidine administration resulted in a lower ($p = 0.03$) lactate concentration during medetomidine administration.

Discussion

In judging the acceptability of a novel measurement technique compared with an accepted or gold standard technique, any differences should lie within clinically acceptable limits of agreement (Bland & Altman 1986). This study demonstrates that pH, PCO_2, SBE and lactate from a LBG sample fall within acceptable limits of agreement with the standard arterial values.

Lactate, pH and PCO_2 measurements from a LBG sample demonstrated a very small overestimation of the arterial value. The range of measured values lie within the normal physiologic range for pH and lactate (Table 1, Figure 1; (Evans 1987; McMichael et al. 2005)). The range of measured values for LBG PCO_2 and arterial PCO_2 included hypercapneic samples due to the tendency for $P_{E'}CO_2$ to underestimate $PaCO_2$, and resulting from the use of normocapnoeic $P_{E'}CO_2$ values as an inclusion factor (Table 1). The limits of agreement for lactate (-0.3, 0.3 mmol L^{-1}), pH (-0.01, 0.02) and PCO_2 (-3.5, 4.6 mmHg [-0.5, 0.6 kPa]) fall within ranges that would not result in a change in therapy. Although the overestimation of ABG by LBG for SBE was small, the limits of agreement are wide, ranging from -1.2 to 2.3 mmol L^{-1}. However, this is unlikely to affect clinical decision making when interpreted in conjunction with pH, pCO_2 and electrolytes.

The underestimation of ABG by LBG for PO_2 (-86.3 mmHg [-11.5 kPa]) and the wide limits of agreement calculated (-199.8, 27.3 [-26.6, 3.6 kPa]; Figure 2), suggest that reliance on LBG for an estimation of ABG may be misleading. The utility of PO_2 measured by LBG as a substitute for ABG in humans has been a source of debate (Barry et al. 1995; Pandit 1995; Dall'Ava-Santucci et al. 1996), due to the variability of results from different studies. In part, this variation is likely due to differences in study design, heterogeneous patient populations, small sample size and inappropriate statistical analysis of results. Study design has differed greatly in

both the aim of the study (tracking of long-term oxygen therapy (Eaton et al. 2001), monitoring under anesthesia (Abou-Madi & Robertson 1988; Wagner et al. 1991), monitoring in an intensive care unit (Escalante-Kanashiro & Tantalean-Da-Fieno 2000; Yildizdas et al. 2004)), method of site preparation and sample site ("arterialisation" of site by vasodilator creams (Dar et al. 1995; Sauty et al. 1996; Eaton et al. 2001) and/ or hot packs (Harrison et al. 1997; Escalante-Kanashiro & Tantalean-Da-Fieno 2000; Eaton et al. 2001) or no site preparation (Rodkey 1978; van Sluijs 1983; Yildizdas et al. 2004)). Population heterogeneity has varied greatly in terms of patient age (Harrison et al. 1997; Escalante-Kanashiro & Tantalean-Da-Fieno 2000; Yildizdas et al. 2004) and underlying disease chronicity and severity (Sauty et al. 1996; Escalante-Kanashiro & Tantalean-Da-Fieno 2000; Eaton et al. 2001) within and between individual studies.

The only two studies in dogs comparing lingual venous blood samples with arterial samples examined data using linear regression analysis and calculation of the correlation coefficient (Abou-Madi & Robertson 1988; Wagner et al. 1991). Both studies reported a significant linear correlation between LBG and ABG in healthy, anesthetized dogs. This approach is limited in that it is difficult to assess the suitability of a new technique in replacing a current technique because limits of agreement cannot be assessed (Bland & Altman 1986). Furthermore, a strong correlation is likely to result from data covering a wide range of values and when two methods measuring the same parameter are investigated. Wagner et al (1991) did assess the presence of bias and identified that LBG underestimated ABG for PO_2 and PCO_2 by approximately 108 mmHg (14.5 kPa) and 5 mmHg (0.7 kPa) respectively. The relationship between arterial pH and lingual pH was described as: pH arterial = (0.97 x pH lingual) + 0.22.

Whilst these findings are similar to those reported here, a comparison is difficult without calculation of the limits of agreement.

It has been suggested in the veterinary literature (Wagner et al. 1991) that a lingual blood gas within the expected range for the delivered fraction of oxygen provides reassurance that hypoxemia is not present. That is, PO_2 measured by an LBG sample cannot overestimate the true ABG value. The results presented here partially support this conclusion. Whilst no LBG sample overestimated the ABG value of PO_2 (Figure 2), the calculated limits of agreement extend into the positive range (Table 1). This finding reflects a limitation of the statistical method applied, however a measurement error resulting in overestimation of ABG by LBG has been reported in the human literature (Langlands & Wallace 1965; Sauty et al. 1996; Harrison et al. 1997; Eaton et al. 2001).

During the experimental arm of the study, minor differences were identified between values of pH sampled from each site. The range of median values spanned 0.06 pH units. These are not of clinical significance, in that they would not alter treatment. Administration of medetomidine resulted in a small decrease in the value of PO_2 sampled from the LBG site (Table 2), which was statistically significant but not clinically significant. These effects may reflect a minimal change in the composition of lingual blood following medetomidine administration. By comparison, the effect of medetomidine on PO_2 from the VBG site sample was marked. Medetomidine administration resulted in a significantly lower PO_2 than during isoflurane alone, likely reflecting the greater oxygen extraction associated with medetomidine administration. These results indicate that LBG samples provide a closer approximation of ABG PO_2 than VBG samples even during medetomidine administration. It is not possible to quantify the difference in

PO_2 with and without medetomidine administration from these data. However, the underestimation of ABG by LBG for PO_2 was within the range calculated from the Bland and Altman analysis of the data from the clinical arm (Tables 1 and 2). Similarly to the findings reported for PO_2, LBG samples of PCO_2 provide a closer approximation of ABG values than VBG during medetomidine administration. The significant effects of medetomidine on both PO_2 and PCO_2 values obtained from jugular venous samples reflect the cardiovascular effects of medetomidine dogs (Murrell and Hellebrekers, 2005; Sinclair 2003). The significant reduction in cardiac output following medetomidine administration may result in greater oxygen extraction, reflected by the low values of venous PO_2. A reduced peripheral perfusion resulting from the combined effects of reduced cardiac output and increased systemic vascular resistance following medetomidine administration could explain the increased venous PCO_2 (Pypendop and Verstegen, 2000). The minimal effect of medetomidine on PO_2 and PCO_2 levels from LBG and ABG samples indicates a greater contribution of arterial than venous blood in LBG samples. It is unclear why medetomidine administration would result in a lower lactate concentration in LBG samples than during isoflurane administration alone. A previous study, during which medetomidine was administered either intravenously (750 μg m^{-2}) or intramuscularly (1000 μg m^{-2}) to unsedated dogs did not identify a significant difference in arterial lactate concentrations (Pettifer & Dyson 1993). To the authors' knowledge, the effect of medetomidine administration on LBG samples has not been previously documented. This effect of medetomidine may reflect a decreased contribution of peripheral tissues to the composition of plasma lactate due to peripheral vasoconstriction. Although samples were not taken, it would have been interesting to have extended the sampling period to the recovery period from medetomidine administration in

order to follow any changes in plasma lactate levels as peripheral perfusion increased. It should be noted that little has been published regarding the interaction of medetomidine and isoflurane. Pypendop and Verstegen (2000) found decreases in skeletal muscle and intestinal blood flow during administration of isoflurane, medetomidine, midazolam and butorphanol.

This study was limited by the healthy population sampled. As a result, the range of blood gas values examined was relatively narrow and the predictive value of LBG was not examined under extremes of oxygenation, perfusion or metabolic rate.

The findings of this study indicate that a lingual venous blood sample is a clinically acceptable substitute for an arterial blood sample for pH, PCO_2, SBE and lactate in the population studied. A limitation of this technique is that it can only be performed in anesthetized or unconscious dogs. Measured values of PO_2 from a lingual venous blood sample should be interpreted with caution and cannot be assumed to provide an acceptable estimation of the arterial value, although no LBG samples overestimated the ABG value in these data. The administration of a medetomidine CRI in isoflurane – anesthetized dogs does not preclude LBG sampling as an alternative to ABG sampling for PO_2, PCO_2, pH and lactate. However, due to the small number of dogs studied, it was not possible to extrapolate these results to a larger population. The utility of LBG sampling as a substitute for ABG sampling in the presence of medetomidine warrants further study.

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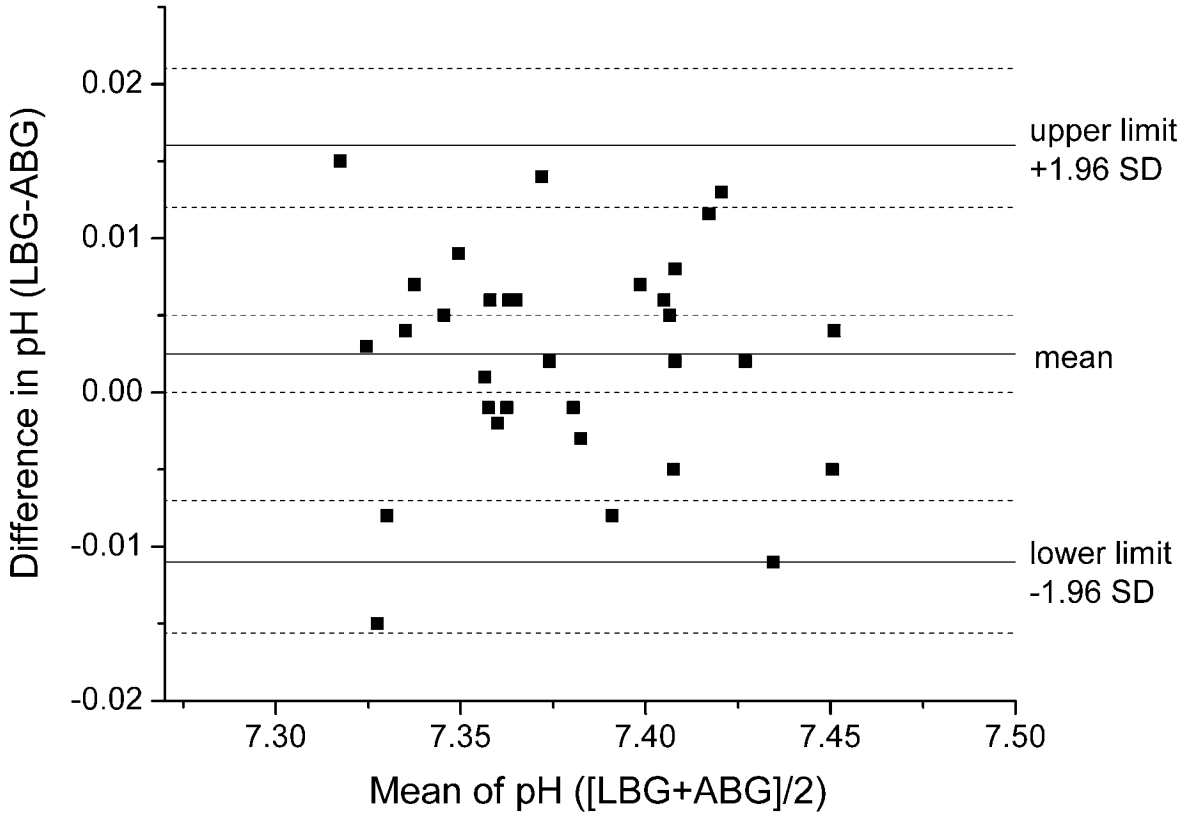
389 **Figures**



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392 Figure 1: Bland–Altman plot illustrating the difference in pH (LBG – ABG) plotted against the
393 mean of pH ([LBG+ABG]/2). The central solid line represents the mean bias of the
394 measurements and the limits of agreement are illustrated by adjacent solid lines (±1.96 SD).
395 Broken lines represent the 95% confidence intervals of the limits of agreement. There are fewer
396 number of points illustrated than analyzed due to replication of points.

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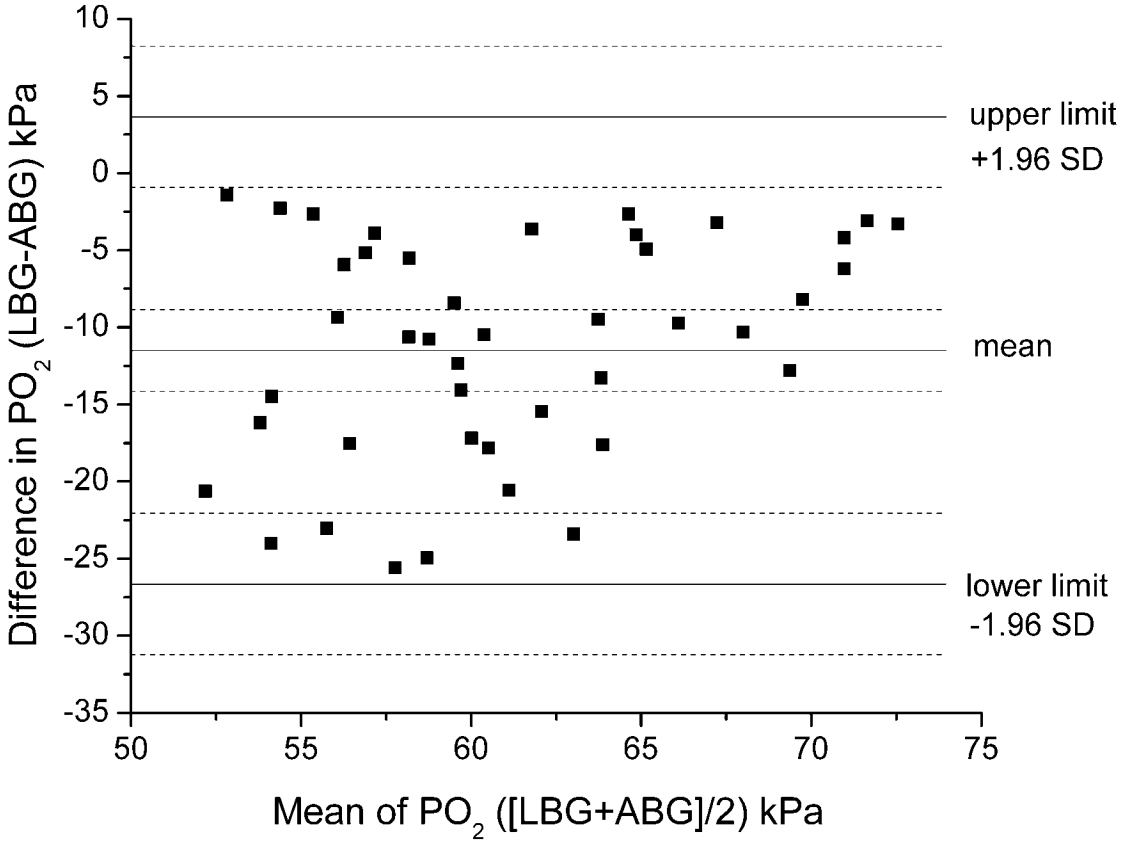

Figure 2: Bland–Altman plot illustrating the difference in PO_2 (LBG – ABG) plotted against the mean of PO_2 ([LBG+ABG]/2). The central solid line represents the mean bias of the measurements and the limits of agreement are illustrated by adjacent solid lines (±1.96 SD). Broken lines represent the 95% confidence intervals of the limits of agreement. There are fewer number of points illustrated than analyzed due to replication of points.

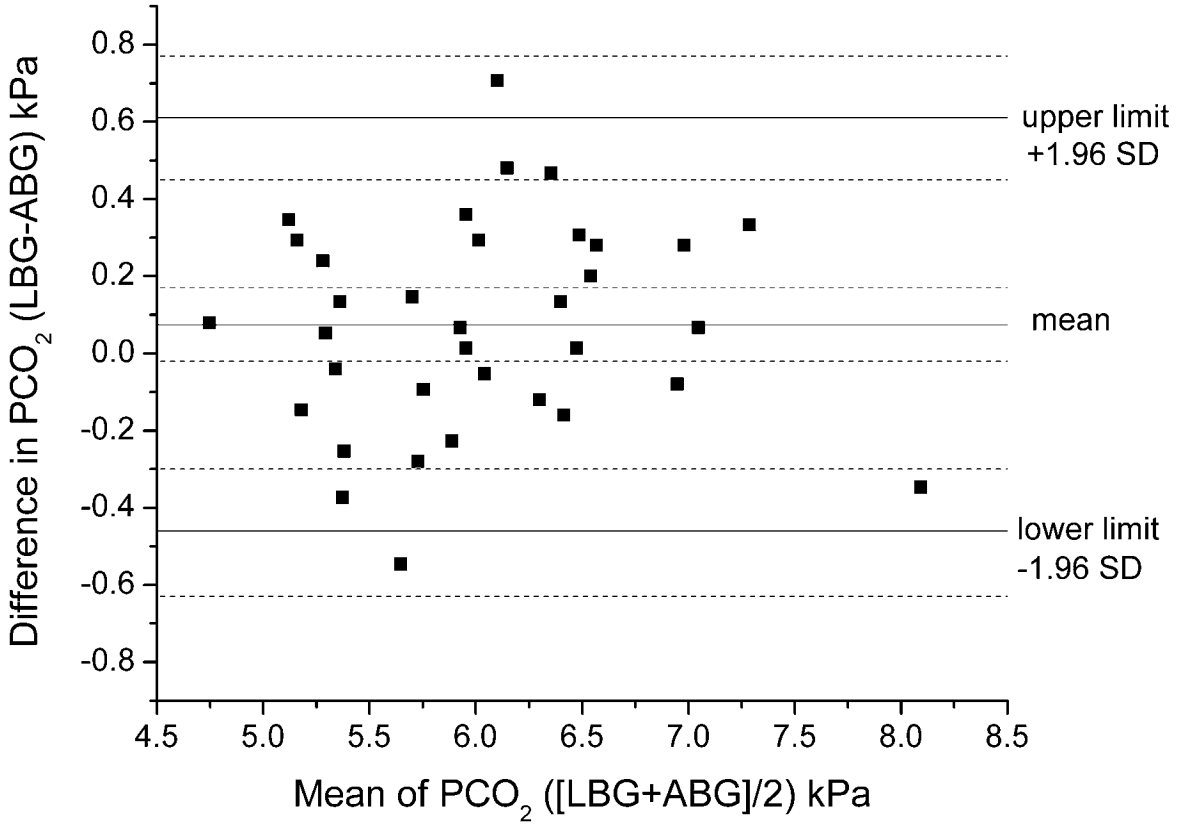

Figure 3: Bland–Altman plot illustrating the difference in PCO_2 (LBG – ABG) plotted against the mean of PCO_2 ([LBG+ABG]/2). The central solid line represents the mean bias of the measurements and the limits of agreement are illustrated by adjacent solid lines (±1.96 SD). Broken lines represent the 95% confidence intervals of the limits of agreement. There are fewer number of points illustrated than analyzed due to replication of points.

Table 1: Results of Bland and Altman analysis of measured and calculated blood gas and electrolyte parameters. CI is confidence interval. SD is standard deviation.

	Bias	CI (95%) of bias	Limits of agreement (±1.96SD)	CI for lower limit	CI for upper limit	Arterial sample median [range]
pH	0.00	(0.00,0.01)	(-0.01, 0.02)	(-0.02, -0.01)	(0.01, 0.02)	7.37 [7.31 – 7.45]
PO_2 (mmHg) {kPa}	-86.3 {-11.5}	(-106.2, -66.4) {-14.2, -8.9}	(-199.8, 27.3) {-26.6, 3.6}	(-234.1, -165.5) {-31.2, -22.1}	(-7.1, 61.6) {-0.9, 8.2}	504.8 [401.3 – 567.8] mmHg 67.3 [53.5 – 75.7] kPa
PCO_2 (mmHg) {kPa}	0.6 {0.1}	(-0.2, 1.3) {-0.0, 0.2}	(-3.5, 4.6) {-0.5, 0.6}	(-4.7, -2.3) {-0.6, -0.3}	(3.4, 5.8) {-0.5, 0.8}	44.3 [35.3 – 62.3] mmHg 5.9 [4.7 – 8.3] kPa
SBE (mmol L^{-1})	0.6	(0.2, 0.9)	(-1.2, 2.3)	(-1.7, -0.6)	(1.8, 2.9)	1.7 [-3.2 – 6.3]
Lactate (mmol L^{-1})	0.0	(-0.0, 0.1)	(-0.3, 0.3)	(-0.4, -0.2)	(0.2, 0.4)	1.4 [0.1 – 5.1]

Table 2: Results from experimental arm of the study following administration of a medetomidine CRI. Values are expressed as median [range]. Significant differences ($p < 0.05$) exist between pairs of data with the same superscript letter within each line.

	isoflurane - LBG	medetomidine – LBG	isoflurane – ABG	medetomidine - ABG	isoflurane - VBG	medetomidine - VBG
pH	7.41 [7.33-7.43]^{a}	7.38 [7.33-7.42]^{c}	7.42 [7.33-7.43]^{b}	7.38 [7.33-7.41]^{d}	7.40 [7.31-7.42]^{a,b,e}	7.35 [7.30-7.39]^{c,d,e}
PO_2 (mmHg) {kPa})	(465.4 [459.0-525.3])^{a,c,g} {62.0 [61.2-70.0]}	(462.6 [300.9-472.2])^{d,e,g} {61.7 [40.1-63.0]}	(548.4 [500.2-577.6])^{a,b} {73.1 [66.7-77.0]}	(558.6 [459.6-581.0])^{d,f} {74.5 [61.3-77.5]}	(207.5 [120.7-281.8])^{b,c,h} {27.7 [16.1-37.6]}	(82.7 [58.9-89.0])^{e,f,h} {11.0 [7.9-11.9]}
PCO_2 (mmHg) {kPa})	(38.1 [36.2-39.1])^{a} {5.1 [4.8-5.2]}	(39.5 [38.9-47.6])^{c} (5.3 {5.2-6.3})	(37.5 [37.1-44.8])^{b} (5.0 {4.9-6.0})	(42.6 [39.0-44.8])^{d} (5.7 {4.0-6.0})	(41.0 [38.3-45.2])^{a,b,e} (5.5 {5.1-6.0})	(47.9 [45.0-48.9])^{c,d,e} {6.4 [6.0-6.5]}
Lactate (mmol L^{-1})	1.4 [0.7-2.0]^{a}	0.8 [0.4-1.3]^{a}	1.2 [0.7-2.0]	1.0 [0.4-1.3]	1.2 [0.7-2.1]	1.0 [0.5-1.3]