Oxygenation status was evaluated in medetomidine-sedated dogs breathing room air (M) or 100% oxygen (MO₂). Medetomidine (40 µg/kg IV) administration resulted in peripheral vasoconstriction and decreased venous saturation as measured by an increased oxygen extraction ratio in peripheral tissues. Providing 100% oxygen insufflation via face mask reduced desaturation by increasing oxygen content but did not prevent vasoconstriction or reduce the oxygen extraction ratio in peripheral tissues. Atipamezole (200 µg/kg IV) reversed medetomidine-induced vasoconstriction and increased oxygen supply to tissues as indicated by a lower tissue oxygen extraction ratio. The authors conclude that 100% oxygen insufflation via face mask during medetomidine sedation (40 µg/kg IV) benefits tissue oxygenation in healthy dogs.
The total amount of oxygen carried in the arterial and venous blood is usually expressed as oxygen content for arterial (CaO₂) and mixed venous (CvO₂) blood. CaO₂ and CvO₂ are influenced by the amount of hemoglobin available to bind oxygen, or hemoglobin saturation for oxygen (SaO₂ [arterial] or SvO₂ [venous]), and the amount of oxygen dissolved in the blood, or partial pressure of oxygen (PaO₂ [arterial] or PvO₂ [venous]). Studies have measured oxygen saturation and partial pressure of oxygen in medetomidine-sedated dogs breathing room air or 100% oxygen.

Atipamezole is a highly specific antagonist for α₂-adrenergic agents such as medetomidine. The effect of atipamezole on CaO₂, CvO₂, and CaO₂ – CvO₂, as well as lactate concentration immediately following reversal of medetomidine, has not been well documented. The purposes of this study were (1) to determine whether there was a decrease in CaO₂ and CvO₂ from peripheral blood following medetomidine administration; (2) to compare CaO₂, CvO₂, CaO₂ – CvO₂, and blood lactate concentrations in medetomidine-sedated dogs breathing room air versus 100% oxygen insufflation via face mask; and (3) to assess the effect of atipamezole reversal of medetomidine on these variables in dogs.

**Materials and Methods**

This experiment was approved by the Oklahoma State University Animal Care and Use Committee and conducted at Oklahoma State University. Seven 2-year-old, mixed-breed hound-type dogs (five females and two males)
were used in this crossover study. Mean (±SD) body weight was 21.2 (±1.8) kg. The dogs were randomly assigned to two treatment groups, breathing either room air (M) or 100% oxygen (MO2) insufflated via face mask (oxygen flow rate: 3 L/min) while under sedation with medetomidine (Domitor; Pfizer Animal Health). All dogs received medetomidine (40 µg/kg IV) via a preplaced venous catheter (BD-Angiocath; The Medical Supply Company, Bethpage, NY). Each dog received both treatments in random order, with a 7-day interval between treatments.

While breathing room air before drug administration, an arterial catheter was inserted into the dorsal pedal artery of all dogs for blood pressure measurement and blood gas sampling and an IV catheter was inserted into a cephalic vein for blood sampling and drug administration. All dogs were connected to an electrocardiograph before any drug was administered, and a lead-II electrocardiogram (ECG) was used to monitor for arrhythmias throughout the experiment. A direct blood pressure transducer (zero reference point set at the level of the right heart) and monitor were used to constantly monitor systolic, diastolic, and mean arterial blood pressures; values were recorded at baseline (time 0) and 2, 5, 10, 20, 25, 30, and 33 minutes after medetomidine administration. Baseline heart rate (HR) and respiratory rate (RR) were measured via direct arterial wave form and chest excursion, respectively. Medetomidine was given immediately after baseline measurements were obtained.

After baseline measurements were recorded and while the animals were breathing room air, dogs were injected with medetomidine (40 µg/kg IV) and then randomly assigned to one of the two treatment groups described above. Atipamezole (200 µg/kg IV) was administered immediately after the 30-minute data were obtained. Arterial and venous blood samples were collected 3 minutes later (i.e., 33 minutes after medetomidine administration).

The color of the mucous membranes and tongue was recorded as pink, cyanotic, or pale at each time point during sedation. Blood samples for lactate concentration and a body temperature–corrected blood gas analysis (i-STAT blood gas analyzer, Heska, Ft. Collins, CO) were obtained immediately after the cardiorespiratory parameters at time zero, 5, 10, 20, 30, and 33 minutes.

Body temperature was monitored using a rectal temperature probe and maintained between 37°C and 39°C using a water-heating blanket, towels, and an insulated table. Packed cell volume (PCV) was determined for each arterial and venous sample. Hemoglobin concentration (Hb) was determined by dividing the PCV by 3.11 and referenced to the Hb value obtained by the blood gas analyzer. CaO2, Cvo2, and peripheral oxygen extraction ratio were calculated using the following equations8,9:

\[
\text{CaO}_2 = (1.36 \times \text{Hb} \times \text{SaO}_2) + (0.0031 \times \text{PaO}_2)
\]

\[
\text{Cvo}_2 = (1.36 \times \text{Hb} \times \text{SvO}_2) + (0.0031 \times \text{PvO}_2)
\]

\[
\text{Oxygen extraction ratio} = \left( \frac{\text{CaO}_2 - \text{Cvo}_2}{\text{CaO}_2} \right) \times 100\%
\]

The cephalic venous blood was used to measure venous oxygen content to examine the peripheral venous tissue oxygenation and periph-

**After medetomidine administration, PaO2 did not change significantly over time in dogs breathing room air.**
eral venous oxygen extraction ratio. The cephalic vein was chosen for ease of access and to examine the peripheral venous oxygenation from a commonly cannulated vessel.

**Statistical Analysis**

Analysis of variance was used to assess treatment differences (PROC MIXED in SAS, Version 8.2; SAS Institute, Cary, NC). When a significant difference \( (P \leq .05) \) was detected between treatment groups, a protected Fisher’s least significant difference test was used for comparison. All results are reported as mean ± SD.

**RESULTS**

There was no significant difference in \( \text{Pa}_02 \) between the two groups while breathing room air at time zero (Figure 1). After medetomidine administration, \( \text{Pa}_02 \) did not change significantly over time in dogs breathing room air (Figure 1). One dog breathing room air had a hypoxemic episode \( (\text{Pa}_02 \text{ of } 59 \text{ mm Hg}) \) 10 minutes after medetomidine injection. All other dogs had \( \text{Pa}_02 \) values between 69 and 93 mm Hg. Following 100% oxygen insufflation, the mean \( \text{Pa}_02 \) increased significantly \( (P < .0001) \) and ranged from 151 to 477 mm Hg during the 30 minutes of sedation (Figure 1). There was no significant difference in the \( \text{Pv}_02 \) values (range: 30 to 53 mm Hg) over time within or between treatment groups (Figure 2).

\( \text{Sa}_02 \) in the M group (measured by blood gas analyzer) was between 92% and 98%, except in the dog with the \( \text{Pa}_02 \) of 59 mm Hg, which had an \( \text{Sa}_02 \) of 89%. \( \text{Sa}_02 \) was 100% in the \( \text{MO}_2 \) group during the 30 minutes of sedation. In contrast, \( \text{Sv}_02 \) in both treatment groups decreased significantly after medetomidine administration (from 80.1% \( [±4.72\%] \) to 64.3% \( [±6.15\%] \) in the M group and from 82.3% \( [±4.1\%] \) to 69.2% \( [±2.5\%] \) in the \( \text{MO}_2 \) group). These values remained lower than baseline values until atipamezole administration (Figure 3).
Mucous membrane color was pale in most of the dogs in the M group. At 5 and 10 minutes, three of the seven dogs had a cyanotic tongue. The color became pinker after 10 minutes. None of the dogs receiving oxygen developed cyanosis.

Throughout the 30-minute period, $\text{CaO}_2$ was significantly higher in the dogs receiving 100% insufflation compared with the dogs breathing room air (Figure 4). Following the start of 100% oxygen insufflation via face mask, $\text{CaO}_2$ increased significantly from baseline. In contrast, $\text{CaO}_2$ decreased significantly after medetomidine administration in the dogs breathing room air (Figure 4). The $\text{CvO}_2$ decreased significantly from baseline after medetomidine administration in both treatment groups until atipamezole administration (Figure 4). $\text{CvO}_2$ was not significantly different between treatment groups.

Both arterial and venous blood lactate concentrations were within the normal reference range (0.6 to 2.9 mmol/dl) for both treatment groups (Figure 5). Neither arterial nor venous blood lactate concentrations changed significantly from baseline following medetomidine administration in either treatment group. However, the blood lactate concentration at 20 minutes was significantly higher ($P < .018$) in venous blood than in arterial blood in the MO group (Figure 5).

Systolic blood pressure did not

Figure 2. Partial pressure of venous oxygen ($P_{\text{vO}_2}$) in medetomidine-sedated (40 µg/kg IV) dogs breathing room air (M) or with 100% oxygen insufflation via face mask (MO<sub>2</sub>). Time 0 was just before medetomidine administration; time 33 was 3 minutes after atipamezole (+A) administration (200 µg/kg IV).

Figure 3. Oxygen saturation in arterial ($S_{\text{aO}_2}$) and venous ($S_{\text{vO}_2}$) blood of medetomidine-sedated (40 µg/kg IV) dogs breathing room air (M) or with 100% oxygen insufflation via face mask (MO<sub>2</sub>). Time 0 was just before medetomidine administration; time 33 was 3 minutes after atipamezole (+A) administration (200 µg/kg IV). Asterisks indicate a significant difference within the group.
increase significantly from baseline values following medetomidine administration. However, diastolic blood pressure significantly increased from the mean baseline values in both treatment groups after medetomidine administration (Figure 6). Heart rate decreased significantly from the mean baseline values following medetomidine administration in both treatment groups (M: 105.7 [±10.6] to 38.7 [±2.5] bpm; MO₂: 101.6 [±12.3] to 51.5 [±8.3] bpm). Respiratory rate did not change significantly from baseline. There was no significant difference between the two treatment groups in heart and respiratory rates at any time point.

Atipamezole administration resulted in an increase in PaO₂ in dogs breathing room air (72.57 [±6.75] to 87.86 [±7.79] mm Hg); however, the increase was not statistically significant. In contrast, SvO₂ increased significantly following atipamezole administration in the room air group (from 75.4% [±3.5%] to 89.7% [±3.4%]) and in the 100% insufflation group (from 79.7% [±5.1%] to 92.5% [±2.8%]). An increase was also observed in Cvo₂ (M: from 17.5 [±0.12] to 20.39 [±0.1] ml/dl; MO₂: from 16.56 [±0.9] to 19.71 [±0.09] ml/dl). Systolic blood pressure did not change significantly immediately before or after atipamezole administration. Diastolic blood pressure, however, was reduced significantly after atipamezole administration. Mucous membrane color went from pale or pale pink to bright pink in all animals breathing room air. Heart rate increased significantly following atipamezole administration; respiratory rate did not change significantly after administration of atipamezole.

Tissue extraction ratio increased significantly at 5 and 10 minutes after medetomidine administration in the group breathing room air. The same was true throughout the sedation period in the group receiving 100% oxygen insufflation. The administration of atipamezole resulted in a significant decrease in tissue oxy-

Figure 4. Oxygen content of arterial (CaO₂) and venous (CvO₂) blood of medetomidine-sedated (40 µg/kg IV) dogs breathing room air (M) or with 100% oxygen insufflation via face mask (MO₂). Time 0 was just before medetomidine administration; time 33 was 3 minutes after atipamezole (+A) administration (200 µg/kg IV). Asterisks indicate a significant difference within the group. Daggers indicate a significant difference between groups.
gen extraction ratio in both treatment groups. This reduction was far lower than the recorded baseline value for each group (Figure 7). All dogs recovered without complications.

**DISCUSSION**

Administration of medetomidine at a dose of 40 μg/kg IV provides sufficient sedation and analgesia for a variety of clinical procedures. Side effects of medetomidine use include hypertension, bradycardia, hypotension, and reduction in cardiac output. This dose (40 μg/kg) was chosen to examine the effects of a higher dose of medetomidine on peripheral tissue oxygenation and blood lactate concentration. The results of this study demonstrate that providing 100% oxygen insufflation during medetomidine sedation prevented the decrease in CaO₂ seen in dogs breathing ambient air. The increase in CaO₂ observed with 100% oxygen insufflation correlated with a significant increase in PaO₂. Although the increase of SaO₂ from baseline following 100% oxygen insufflation was not statistically significant, this increase could be physiologically significant and a contributor to the significant increase in CaO₂. The majority of oxygen in blood is carried by hemoglobin, and even a small increase in SaO₂ correlates with an increase in CaO₂—more so than does an increase in PaO₂. An increase in CaO₂ can provide a wider safety margin to dogs sedated with medetomidine by providing a larger amount of available oxygen to tissues for oxygen extraction. The potential beneficial effect of 100% oxygen insufflation during medetomidine sedation is made evident by the significantly higher tissue oxygen extraction ratios observed throughout the sedation period (Figure 7). This observation was also accompanied by lower arterial blood lactate concentrations in the sedated dogs receiving oxygen insufflation versus those breathing room air.

It has been suggested that the bluish tongue and mucous membrane color of medetomidine-sedated dogs is due to peripheral vasoconstriction resulting in low blood flow through peripheral capillary beds and decreased venous saturation. In this study, cyanosis was observed only in the dogs breathing room air and was not evident in dogs insufflated with 100% oxygen via face mask. Evidently, to observe medetomidine-induced cyanosis in the dogs in this study, a significant reduction in CaO₂ was necessary in addition to decreased venous saturation and vasoconstriction. Furthermore,
cyanosis occurred only when $\text{CaO}_2$ was lowest (5 to 10 minutes after medetomidine administration) during the 30-minute sedation period. Providing 100% oxygen insufflation significantly increased the $\text{PaO}_2$ value and resulted in higher $\text{CaO}_2$, evidently preventing cyanosis. This occurred despite a significant reduction in venous saturation (as evident by significant decreases in $\text{SvO}_2$ and $\text{CvO}_2$) and medetomidine-induced vasoconstriction.

Although medetomidine administration in healthy dogs breathing room air did not cause a statistically significant decrease in either $\text{PaO}_2$ or $\text{SaO}_2$, together their reduction resulted in a significant reduction in $\text{CaO}_2$ for at least 10 minutes. This $\text{CaO}_2$ reduction resulted in reduced oxygen availability to the peripheral tissues, evidenced by a significant increase in arterial blood lactate concentrations. This could be a critical disadvantage in compromised clinical patients. Based on the results of this study, we suggest the administration of 100% oxygen to help prevent a further decrease in $\text{CaO}_2$ when cyanosis occurs following medetomidine administration.

In the current study, the oxygen extraction ratio increased significantly following medetomidine administration in both treatment groups and coincided with a significant increase in blood pressure, especially diastolic blood pressure. This observation supports the hypothesis that medetomidine-induced peripheral vasoconstriction results in a lower blood flow through peripheral capillary beds, leading to decreased venous saturation. The continued increase in oxygen extraction ratio in the group receiving oxygen versus the group breathing room air throughout the sedation period (30 minutes) is intriguing. We hypothesize the larger oxygen extraction ratio simply reflects the increase in $\text{PaO}_2$ and $\text{SaO}_2$—and thus $\text{CaO}_2$—associated with 100% oxygen insufflation, making arterial oxygen supply more readily accessible for tissue extraction. The increase in oxygen availability enables tissues to extract more oxygen to meet metabolic oxygen demand, hence the larger extraction ratio.

Blood lactate has been used to monitor tissue perfusion and tissue oxygenation. Lactate concentration is most commonly elevated with tissue hypoperfusion and hypoxia. Normal blood lactate concentration in dogs is suggested to be less than 2.5 mmol/dl. Values between 5 and 7 mmol/dl are considered moderately elevated, and values above 7 mmol/dl are considered severely elevated. In this study, all lactate concentrations obtained from the cephalic vein and the dorsal metatarsal artery were less than 2.5 mmol/dl at any time, indicating that the medetomidine-
sedated dogs were not hyperlactatemic, regardless of treatment group. This is in agreement with previous work measuring lactate levels in dogs sedated with a lower dose of medetomidine.\textsuperscript{16}

Following medetomidine administration, no significant increases in blood lactate were observed in either arterial or venous blood in both treatment groups. All blood lactate concentrations were within physiologic reference ranges, which potentially indicate that there was no tissue hypoxia–induced hyperlactatemia and may partially explain why clinically healthy dogs sedated with medetomidine and breathing room air recover without serious consequences despite the appearance of cyanosis. The duration of medetomidine sedation in this study was 30 minutes; it is unknown what effect a longer period of sedation may have on subsequent anaerobic metabolism and blood lactate concentration.

Atipamezole is a specific $\alpha_2$-adrenergic antagonist and is frequently used to reverse medetomidine. As expected, atipamezole reversal induced vasodilation and significantly reduced diastolic blood pressure. The vasodilation following atipamezole administration allows more oxygen to become available for tissue extraction than can be used. This was evident in the present study by a significantly lower oxygen extraction ratio and a much higher \( \text{CvO}_2 \) and \( \text{SvO}_2 \), which explains why there is such a dramatic change to a bright pink mucous membrane color immediately following atipamezole reversal of medetomidine. Furthermore, atipamezole administration significantly reduces the venous blood lactate concentration evident during medetomidine sedation, indicating a reduction in oxygen deprivation.

\section*{CONCLUSION}

Based on the results of this study, we conclude that (1) medetomidine administration resulted in peripheral vasoconstriction and increased venous desaturation via an increase in peripheral tissue oxygen extraction; (2) providing 100\% oxygen via face mask prevented blood desaturation by increasing \( \text{CaO}_2 \) but did not influence vasoconstriction nor the increased oxygen extraction ratio in the peripheral tissue; and (3) atipamezole reversed medetomidine-induced vasoconstriction and increased oxygen supply to peripheral tissues as indicated by a lower tissue oxygen extraction ratio. We conclude that the provision of 100\% oxygen via insufflation with a face mask benefits tissue oxygenation in dogs sedated with medetomidine.

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