Comparison of time to desaturation between preoxygenated and nonpreoxygenated dogs following sedation with acepromazine maleate and morphine and induction of anesthesia with propofol

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Objective—To compare the time to desaturation in healthy dogs that breathed oxygen or room air for 3 minutes before induction of anesthesia.

Animals—20 healthy dogs.

Procedures—Dogs were sedated with morphine and acepromazine maleate. Dogs received a 3-minute treatment of room air or oxygen (100 mL/kg/min) via face mask. Arterial blood samples were collected before and after treatment to determine $Paco_2$, Pao_2, pH, and Sao_2; propofol (6 mg/kg, IV) was injected during a 7-second period, and the dogs were intubated. A lingual pulse oximeter probe was placed. Dogs remained disconnected from the breathing circuit until Spo_2 equaled 90% (desaturation point) and then connected and ventilated until the Spo_2 was $\geq$ 97%. Arterial blood samples were collected and Spo_2 was recorded every 30 seconds for 4 minutes and then every minute until the desaturation point. Times to first breath and the desaturation point were recorded. Data were collected at 0, 5, 30, 60, 90, 120, and 150 seconds.

Results—Mean ± SEM time to desaturation differed significantly between dogs treated with room air (69.6 ± 10.6 seconds) and oxygen (297.8 ± 42.0 seconds). Lowest mean Pao_2 and Sao_2 when dogs were breathing room air were 62 ± 6.3 mm Hg and 82.3 ± 4%, respectively, at 30 seconds.

Conclusions and Clinical Relevance—Preoxygenation for 3 minutes increased the time to desaturation in healthy dogs sedated with acepromazine and morphine in which anesthesia was induced with propofol. (*Am J Vet Res* 2009;70:1333–1338)

H ypoxemia (Pao_2 < 60 mm Hg or Sao_2 < 90%)[1] can develop even in healthy human patients during induction of anesthesia.[2] Causes of hypoxemia include low inspired oxygen concentration, alveolar hypoventilation, diffusion abnormalities, ventilation-perfusion mismatch, and shunting.[3] Conditions that predispose a patient to hypoxemia at induction of anesthesia include respiratory depression, reduced FRC, or reduced cardiopulmonary function.[4] Apnea or respiratory obstruction during induction can exacerbate preexisting respiratory problems.

ABBREVIATIONS

A-a	Alveolar to arterial
Feo_2	Fraction of expired oxygen
Fio_2	Fraction of inspired oxygen
FRC	Functional residual capacity
$Petco_2$	End-tidal partial pressure of carbon dioxide
Sao_2	Saturation of arterial hemoglobin measured with a co-oximeter
Spo_2	Saturation of arterial hemoglobin measured with a pulse oximeter

Delivery of oxygen before induction of anesthesia (preoxygenation) is routine for anesthesia in humans, especially in certain patient populations, including obese patients, pregnant patients, and patients with expected airway difficulties.[5,6] In theory, preoxygenation replaces alveolar nitrogen with oxygen to achieve an intrapulmonary oxygen reserve.[7] Hemoglobin becomes fully saturated, and dissolved oxygen increases. The goal is to increase the interval to onset of hypoxemia. Even partial alveolar denitrogenation will increase the safety margin in preventing hypoxia at induction of anesthesia.[8]

Numerous studies[2,9–13] have been conducted in human medicine to determine the general effectiveness of preoxygenation and the effectiveness of specific meth-

ods of preoxygenation. Methods used have included 1 to 5 minutes of tidal volume breathing or inspiratory capacity breaths taken over a certain time period (eg, 4 breaths in 30 seconds or 8 breaths in 60 seconds). Although most of these studies have detected a benefit to preoxygenation in guarding against hypoxemia, 1 study[14] performed on critically ill patients revealed only minimal improvement in arterial oxygen tension prior to intubation. In other studies, investigators have evaluated changes in Pa_{CO_2} with onset of experimentally induced apnea and obstruction[15] and the formation of atelectasis at induction of anesthesia,[16] which has been linked to breathing high concentrations of oxygen.

Veterinary medicine has adopted the practice of preoxygenation for specific situations, including brachycephalic patients[17] and patients undergoing cesarean section.[18] However, to the authors' knowledge, there have been no published reports on the outcome of preoxygenation in dogs. The optimal time for preoxygenation as well as the time until desaturation following preoxygenation is unknown. The purpose of the study reported here was to compare the time to desaturation between preoxygenated and nonpreoxygenated healthy dogs in a controlled setting by use of 3 minutes of tidal volume (spontaneous) breathing, which is the most traditional method of preoxygenation in human medicine. In addition, the Pa_{O_2}, Sa_{O_2}, Pa_{CO_2}, and pH were compared between the 2 groups.

Materials and Methods

Animals—Twenty sexually intact (10 males and 10 females) mixed-breed dogs were used in the study. Dogs were between 6 months and 3 years of age and weighed (mean ± SEM) 23.0 ± 2.2 kg. All dogs were determined as healthy on the basis of results of a physical examination and were scheduled for ovariohysterectomy or castration. No hematologic analysis was performed prior to administration of premedication. The Institutional Animal Care and Use Committee of the University of Florida approved the experimental protocol.

Study design and treatments—Each animal was premedicated with acepromazine maleate (0.05 mg/kg, IM) and morphine (0.5 mg/kg, IM). The hair over the left or right dorsal pedal artery was clipped, and topical anesthetic cream[a] was applied, which was followed by application of an occlusive bandage. Thirty minutes after administration of premedication, a 20-gauge, 1.25-inch catheter was placed in the left or right cephalic vein. A 20- or 22-gauge, 1.25-inch catheter was placed percutaneously in the prepared dorsal pedal artery. A baseline arterial blood sample (1 mL; time 0) was collected in a heparinized syringe[b] and placed on ice until analyzed. At the same time, a baseline pulse oximeter[c] measurement was obtained from the lip or the area between the toes, depending on patient compliance. Dogs were randomly assigned by coin toss to 1 of 2 treatment groups. The room air group (n = 10 dogs) breathed room air through a face mask for 3 minutes, whereas the preoxygen group (10) received oxygen (100 mL/kg/min) through a face mask for 3 minutes. Room air and oxygen were delivered by use of a standard anesthetic circle system. A transparent, cone-shaped, medium face mask was modified with memory foam to improve the comfort and seal between the mask and each dog's face. Gas samples were collected from the connector end of the face mask and channeled to a patient monitor[d] for measurement of Pet_{CO_2}, Fi_{O_2}, and Fe_{O_2} during the treatment. The monitor was calibrated at the beginning and end of the study by use of a standardized calibration gas[e] designed for the analyzer. Apparatus dead space was minimal, and at no time did the monitor indicate rebreathing of carbon dioxide.

After the 3-minute treatment, dogs were injected with propofol (6 mg/kg), which was administered as a rapid IV bolus (50 mg/kg/min) during a 7-second period. Propofol was administered through the cephalic catheter, and dogs were then intubated with an appropriately sized, cuffed endotracheal tube. The pulse oximeter was placed on each dog's tongue as soon as possible after induction. Results for the pulse oximeter served as the assessment for time to desaturation, with a predetermined end point of $Sp_{O_2} \leq 90\%$. Dogs were not connected to the breathing circuit until the desaturation point was achieved. Another blood sample was collected immediately after induction (time = 5 seconds) and every 30 seconds for 4 minutes, after which blood samples were collected every minute. Once the desaturation point was achieved, the dogs were connected to the breathing circuit and ventilated with an oxygen flow rate of 100 mL/kg/min until an Sp_{O_2} of 97% was achieved. A final blood sample was collected at that point; all blood samples were stored on ice and analyzed within 15 minutes after collection. Time to first breath was recorded when applicable. Propofol boluses (0.5 mg/kg, IV) were administered as needed during the desaturation period to maintain an adequate plane of anesthesia, as determined on the basis of lack of jaw tone and minimal palpebral reflexes.

Blood gas analysis—Arterial blood samples were analyzed for Pa_{O_2}, Pa_{CO_2}, and pH by use of a blood gas analyzer.[f] Samples from the final 10 dogs (5 dogs of each treatment group) were analyzed for lactate content with the same blood gas analyzer. A veterinary co-oximeter[g] calibrated for dogs was used to measure hemoglobin and Sa_{O_2}. The machines were calibrated at the beginning of each study day.

Statistical analysis—All data were reported as mean ± SEM. The errors were distributed normally. Data for time to desaturation were analyzed with an unpaired t test. Because of missing data points after 150 seconds for the room air group (all dogs in the room air group had desaturated by that point), only data from baseline up to 150 seconds were analyzed for Pa_{O_2}, Pa_{CO_2}, pH, lactate concentration, and Sa_{O_2}. These measurements were analyzed with unpaired t tests between dogs and paired t tests within dogs; values for dogs of each group were compared with baseline values. A Bonferroni t test was used for these multiple comparisons over time. For unpaired t tests, a value of $P \leq 0.05$ was considered significant, whereas for the Bonferroni t test, a critical value of $P = 0.05/6 = 0.008$ was used.

Results

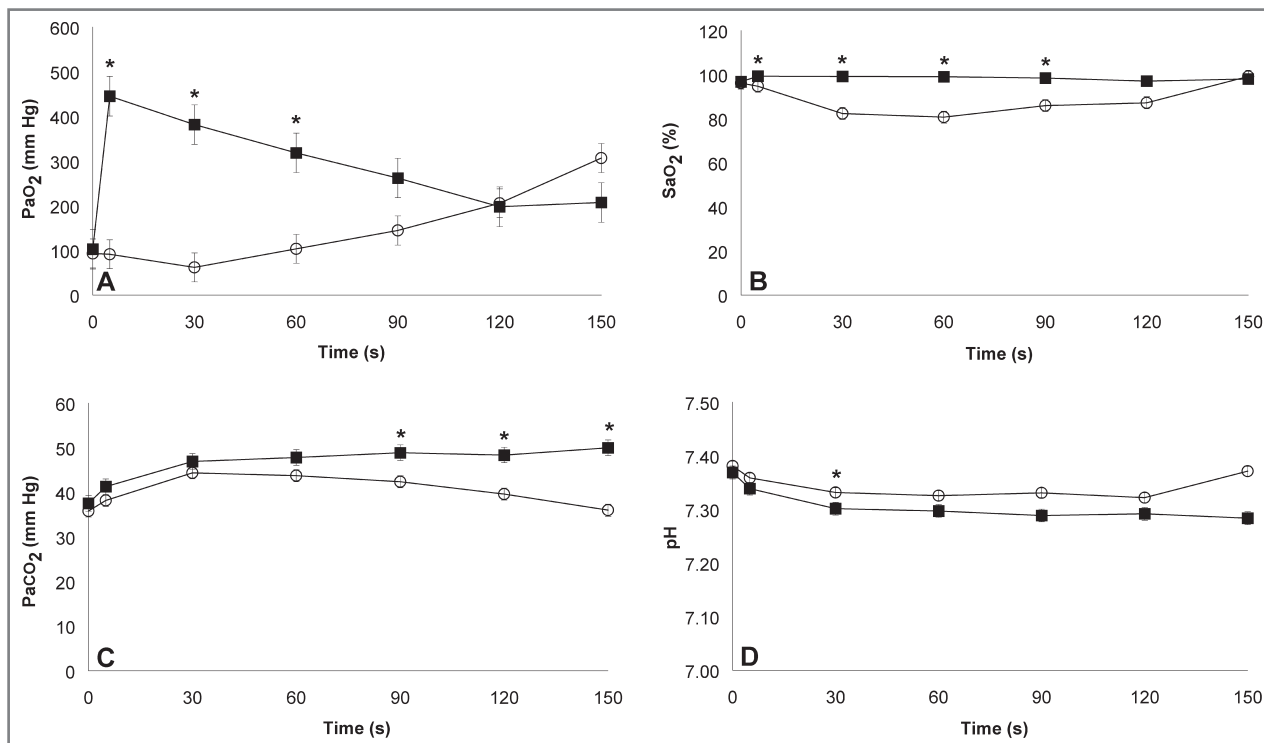Mean ± SEM measured Fi_{O_2} of preoxygenated dogs at the end of treatment was 0.88 ± 0.020. The Fi_{O_2} of

Figure 1—Mean ± SEM values for Pao_2 (A), Sao_2 (B), $Paco_2$ (C), and pH (D) over time after induction of anesthesia following a 3-minute treatment via face mask with room air (white circles) or 100% oxygen (black squares). Time 0 = Start of the 3-minute treatment (baseline). *Within a time point, values differ significantly ($P \leq 0.05$) between the treatments.

room air dogs was 0.21 ± 0.002. The Feo_2 of preoxygenated dogs was 0.82 ± 0.020. The Feo_2 of room air dogs was 0.17 ± 0.003.

Except for the short-term hypoxemia, no untoward effects were detected at any point during the study. All dogs recovered uneventfully after surgery. Mean ± SEM baseline hemoglobin concentration was 10.5 ± 0.6 g/dL and 10.2 ± 0.4 g/dL for preoxygenated and room air dogs, respectively. There were no significant differences between the 2 groups at baseline for Pao_2, $Paco_2$, Sao_2, pH, hemoglobin concentration, or lactate concentration. Total propofol dose for induction was 6 mg/kg for each dog. No dogs reacted to intubation. No dogs in the room air group received additional propofol. One dog in the room air group took a breath immediately after induction, whereas 3 room air dogs took their first breaths at 10, 64, and 77 seconds. The remaining 6 room air dogs were apneic. Several dogs in the preoxygenated group received additional doses of propofol, but not during the first 150 seconds. The total additional amount of propofol for the preoxygenated group was not recorded. All dogs in the preoxygenated group were apneic immediately after induction, with a range of 67 to 390 seconds for time until the first spontaneous breath.

Time to desaturation differed significantly ($P < 0.001$) between the 2 groups. Mean ± SEM time to desaturation based on an Spo_2 of $\leq 90\%$ was 288 ± 42.0 seconds (range, 120 to 520 seconds) for the preoxygenated group, whereas the mean time to desaturation for the room air group was 70 ± 11 seconds (range, 40 to 140 seconds). Values for Pao_2, Sao_2, $Paco_2$, and pH were

plotted (**Figure 1**). Significant differences between the 2 groups were detected for Pao_2 at 5, 30, and 60 seconds. Because of a large variance, there were no significant differences in Pao_2 for the room air group at any time, compared with the Pao_2 at baseline. The Pao_2 of the room air group increased after the 30-second time point because most of the room air dogs had desaturated and were being ventilated with 100% oxygen at that point (range, 40 to 140 seconds). The lowest mean Pao_2 of the room air group was 62 ± 6.3 mm Hg at the 30-second time point. Values for Pao_2 increased significantly, compared with the baseline value, for the preoxygenated group at 5, 30, and 60 seconds. Values for Pao_2 then had a downward pattern, but no dogs were hypoxemic (Pao_2 < 60 mm Hg or Sao_2 < 90%) during the 150-second interval.

Significant differences between the 2 groups for Sao_2 were detected at 5, 30, 60, and 90 seconds. There were no differences in Sao_2 in the room air group at any time points, compared with the baseline Sao_2. Values for Sao_2 increased significantly, compared with the baseline value, for the preoxygenated group at 5, 30, and 60 seconds. Mean ± SEM Sao_2 of room air dogs was $\leq 90\%$ at the 30-second time point (actual value, 82.3 ± 4%), whereas the time to desaturation based on an Spo_2 $\leq 90\%$ was 70 ± 11 seconds.

Significant differences between the 2 groups for $Paco_2$ were detected at 90, 120, and 150 seconds. Values for $Paco_2$ increased significantly, compared with the baseline value, for the preoxygenated group at 5, 30, 60, 90, and 150 seconds. The $Paco_2$ increased significantly, compared with the baseline value, for the room air group at 5, 30, 60, and 120 seconds.

Significant differences between the 2 groups for pH were detected at 30 and 150 seconds. The pH of the room air group decreased significantly, compared with the baseline pH, at 5, 30, and 60 seconds. The pH of the preoxygenated group decreased significantly, compared with the baseline pH, at 5, 30, 60, 90, 120, and 150 seconds.

No significant differences were detected between or within groups for lactate or hemoglobin concentrations at any time point.

Discussion

Results of the study reported here indicated that preoxygenation for 3 minutes prior to induction of anesthesia increased the time to desaturation of hemoglobin in healthy dogs. This finding agrees with findings in similar studies[2,10,11] conducted on human patients by use of similar methods of preoxygenation. The mean ± SEM time to desaturation ($Sp_{O_2} \leq 90\%$) in preoxygenated dogs was 297.8 ± 42.0 seconds, whereas the mean time to desaturation in dogs that received room air was 69.6 ± 10.6 seconds. The mean Sa_{O_2} of dogs that received room air was $82.3 \pm 4\%$ within 30 seconds.

In a physiologic modeling study[19] conducted in humans to examine the onset and course of hypoxemia during apnea after pulmonary denitrogenation, several factors were found to have an impact on time to desaturation. Factors that had an effect were increased oxygen consumption (pyrectic or pregnant patients) and reduced FRC. Reduced FRC may be a result of reduced thoracic compliance, increased intra-abdominal pressure, or induction of anesthesia. In 1 study[20] in human patients, investigators found that induction of anesthesia causes a 50% reduction in FRC. Therefore, we hypothesize that the rapid onset of hypoxemia in room air dogs was primarily attributable to reduced FRC from induction of anesthesia with no intrapulmonary oxygen reserve or increased oxygen dissolved in plasma. The cause of reduced FRC as a result of induction of anesthesia is unclear but may involve altered thoracic cage recoil,[21] cranial displacement of the diaphragm,[22] and redistribution of the intrathoracic blood volume.[23] Reduction in FRC has been reported with inhalant anesthetics,[24] barbiturates,[25] and propofol[26] but not when ketamine is used as an induction agent.[27]

In the study reported here, induction of anesthesia was achieved with a rapidly administered bolus of propofol, with the end result that most dogs were apneic. This was used to simulate a scenario at induction involving an apneic animal in which the intubation and provision of high concentrations of oxygen are delayed. In clinical practice, it is recommended that propofol be injected slowly and to effect. The manufacturers recommend a rate of 7 mg/kg/min to prevent apnea. In 1 study,[28] 85% of dogs became apneic when propofol was injected at a rate of approximately 50 mg/kg/min (approx 6 mg/kg during a 7-second period), which was the rate we used. Therefore, it may be argued that dogs in a clinical setting may be less prone to developing hypoxemia because they are less likely to become apneic during induction. However, the mean Pa_{CO_2} of the room air group at the 30-second time point was 44.4 ± 2.2 mm Hg. The alveolar partial pressure of oxygen (ie, P_{AO_2}) of

these dogs can be estimated on the basis of the following alveolar gas equation:

$$P_{AO_2} = ([PB - P_{H_2O}] \times F_{IO_2}) - (Pa_{CO_2}/R)$$

where PB is the barometric pressure at sea level (ie, 760 mm Hg; this study was conducted at sea level), P_{H_2O} is the water vapor pressure at 37°C (ie, 47 mm Hg), and R is the respiratory exchange ratio, which is assumed to be 0.9 in dogs.[29] The approximate P_{AO_2} of the room air group based on this equation was 100 mm Hg. The mean measured Pa_{O_2} at this time point was 62 ± 7 mm Hg, given an A-a gradient of approximately 38 mm Hg. The typical A-a gradient at an F_{IO_2} of 0.21 during conscious, spontaneous breathing is 5 mm Hg.[30] This indicated that the hypoxemia was not attributable to hypoventilation alone. Typically, the A-a gradient will increase with right-to-left shunting, low mixed-venous oxygen saturation, ventilation-perfusion mismatch, or diffusion impairment.[30] There is no reason to suggest that these healthy dogs had right-to-left shunting or a low mixed-venous oxygen saturation. Additionally, these dogs had Pa_{O_2} values within the reference range prior to induction, which indicated normal gas exchange. The most likely explanation is development of a ventilation-perfusion mismatch attributable to reduced FRC during induction of anesthesia.

The other important variable to consider was Pa_{CO_2}, which affects blood pH. In this study, most dogs were apneic or hypoventilating, as indicated by the increase in Pa_{CO_2} over time in the preoxygenated group. Although not significantly different, preoxygenated dogs typically had a higher Pa_{CO_2} than did room air dogs after induction. Also, preoxygenated dogs typically were more acidotic than were room air dogs, with a significant difference between groups at 30 seconds. These differences were logical after the 60-second time point when most room air dogs were being ventilated and most preoxygenated dogs were not, but even prior to this point, preoxygenated dogs typically had a higher Pa_{CO_2} and lower pH. This finding is similar to the findings of 2 studies[15,31] reported in the human literature. In those studies, although the investigators did not compare preoxygenated and room air groups, the Pa_{CO_2} of the preoxygenated patients increased faster than expected, as determined on the basis of the contribution of metabolic carbon dioxide. There was also an increasingly positive difference between Pa_{CO_2} and Pv_{CO_2}, with a corresponding decrease in pH.[31] These findings were thought to be the result of the Christiansen-Douglas-Haldane effect. Briefly, the Christiansen-Douglas-Haldane effect states that oxygenated hemoglobin has a reduced binding capacity for carbon dioxide, compared with the binding capacity of deoxygenated hemoglobin. During the condition of hyperoxic apnea, the Pa_{CO_2} will not approximate the Pv_{CO_2} and will even exceed it. In the study reported here, Pv_{CO_2} was not measured, so it is unknown whether this effect was the cause for the higher Pa_{CO_2} values in the preoxygenated dogs. Regardless of the mechanism, acidemia of the preoxygenated dogs was not clinically important during the first 150 seconds and would have easily been remedied via positive-pressure ventilation.

Another possibility for decreased pH that was examined in this study was development of lactic acidosis from anaerobic metabolism at the tissue level. In the first 10 dogs of this study, the pH of preoxygenated dogs was significantly lower than that of the room air dogs at several time points after induction. This was thought to be attributable to a pattern for an increased Pa_{CO_2} in the preoxygenated dogs, compared with the Pa_{CO_2} for the room air dogs. However, to rule out the possibility of lactic acidosis, the lactate concentration was measured in the subsequent 10 dogs. No significant differences were detected in lactate concentration between the 2 groups.

Three minutes of tidal volume breathing appeared to achieve adequate denitrogenation in the healthy dogs used in this study; however, it may not be sufficient in patients with pulmonary disease or with a reduced FRC. In 1 study,[8] the end point for adequate preoxygenation was defined as Fe_{O_2} of 90%, which corresponds to an alveolar nitrogen concentration of 5% (with 5% Pet_{CO_2}). In that study,[8] the authors calculated that by ensuring an Fe_{O_2} of 90% and assuming a value within the reference range for human FRC, the oxygen store would be approximately 2 to 2.5 L. With a mean oxygen consumption of 250 to 300 mL/min, this may provide adequate oxygenation during apnea for up to 5 minutes. However, in that study with human patients undergoing routine surgical procedures, 23% of the patients required > 3 minutes for adequate preoxygenation, with 4% of the patients requiring > 5 minutes. The investigators in that study attempted to use assessment of patient factors to determine preoxygenation time. The patient characteristics used included age, sex, weight, and height (all of which could be used to calculate FRC), but only a weak correlation was found. They concluded that patients undergoing routine surgical procedures do not follow the expected patterns of alveolar denitrogenation. However, alveolar denitrogenation of 95% may not be necessary because even partial alveolar denitrogenation will delay the onset of hypoxemia. In the study reported here, the mean Fe_{O_2} of preoxygenated dogs at the end of preoxygenation was 0.82 ± 0.02, and a significant difference in time to desaturation was still detected.

The values for time to desaturation in our study were based on Sp_{O_2} measurements, which admittedly may have been altered by factors such as poor peripheral perfusion, patient movement, extraneous light interference (such as from external fluorescent lighting), or patient pigmentation.[32] The criterion-referenced standard for arterial oxygen saturation is considered to be results obtained by co-oximetry. Therefore, in addition to Sp_{O_2} measurements obtained by use of a pulse oximeter, a co-oximeter was used in this study to measure Sa_{O_2}. By use of this measurement, the mean Sa_{O_2} of the room air group was ≤ 90% at the 30-second time point (actual mean value, $82.3 \pm 4\%$). Therefore, use of the pulse oximeter missed a potentially critical period of hypoxemia in the room air group because the time to desaturation based on Sp_{O_2} was 69.6 seconds. Part of this difference can be explained by a delay in placement of the pulse oximeter probe because it was not securely placed until each dog was intubated. Additionally, pulse oximeters have an inherent delay in displaying a measurement because of signal averaging for each pulse oximeter. The signal averaging time for the pulse oximeter[c] used in this study was 6 to 7 seconds.[h]

Reduction in FRC at induction of anesthesia can result in airway closure as closing capacity of the lungs is approached.[33] This raises an important question regarding the negative aspect of preoxygenation. High concentrations of oxygen will encourage collapse of alveoli with low ventilation-perfusion ratios,[33] which leads to atelectasis; however, the incidence of postoperative complications from development of atelectasis is unknown.[34] Despite this, preoxygenation with 100% oxygen is still routinely used in anesthesia of humans, although it is often followed by ventilation with a lower Fi_{O_2} in an attempt to stop the progression of atelectasis. Also, other methods of preoxygenation have been researched in human anesthesia patients in an attempt to prevent the initial development of atelectasis.[17] Use of a lower Fi_{O_2} during preoxygenation may prevent atelectasis formation, but it reduces the margin of safety when a potentially long period of apnea may develop because of difficulties in airway management.

Patient compliance is an important factor in the success of preoxygenation in dogs. Unless adequately sedated, some dogs do not tolerate a face mask for preoxygenation. If a dog becomes agitated and struggles, this may actually increase oxygen consumption and further decrease the time to desaturation. Modification of the face mask with memory foam subjectively made the mask more tolerable to the study dogs. All dogs tolerated application of the face mask.

Preoxygenation can be beneficial in healthy dogs premedicated with acepromazine and morphine and induced with propofol by increasing the time to desaturation, which is useful when a delay in intubation is encountered. Dogs receiving room air for 3 minutes desaturated quite rapidly, with some dogs becoming hypoxemic within 30 seconds. However, critical periods of hypoxemia may be missed in clinical situations in which an animal is quickly attached to a breathing circuit after intubation and ventilated with 100% oxygen before a pulse oximeter is placed. The negative clinical outcome of this brief episode of hypoxemia is unknown. Preoxygenation may also contribute to a slight increase in Pa_{CO_2} and pH, although these changes are minor and not likely clinically important. On the basis of the rapidity with which dogs receiving room air desaturated in this study, the use of preoxygenation in dogs with an expected decrease in FRC (eg, obese patients or pregnant patients), expected airway difficulties (eg, brachycephalic breeds), and decreased cardiopulmonary function is recommended.

g.   Radiometer OSM-3 Hemoximeter, Radiometer America Inc, Westlake, Ohio.

h.   Technology support, Nellcor Puritan Bennett, Pleasanton, Calif: Personal communication, 2008

References

1.   Shapiro BA, Peruzzi WT. Interpretation of blood gases. Monitoring. In: Ayres SM, ed. *Textbook of critical care.* 3rd ed. Philadelphia: Saunders, 1995;234–331.

2.   Kung MC, Hung CT, Ng KP, et al. Arterial desaturation during induction in healthy adults: should preoxygenation be a routine? *Anaesth Intensive Care* 1991;19:192–196.

3.   West JB. Ventilation-perfusion relationships. In: West JB. *Respiratory physiology.* 7th ed. Baltimore: Lippincott Williams & Wilkins, 2005;55–73.

4.   Thorpe CM, Gauntlett IS. Arterial oxygen saturation during induction of anaesthesia. *Anaesthesia* 1990;45:1012–1015.

5.   Shenkman Z, Shir Y, Brodsky JB. Perioperative management of the obese patient. *Br J Anaesth* 1993;70:349–359.

6.   Byrne F, Oduro-Dominah A, Kipling R. The effect of pregnancy on pulmonary nitrogen washout. A study of pre-oxygenation. *Anaesthesia* 1987;42:148–150.

7.   Editorial. Preoxygenation: physiology and practice. *Lancet* 1992;339:31–32.

8.   Machlin HA, Myles PS, Berry CB, et al. End-tidal oxygen measurement compared with patient factor assessment for determining preoxygenation time. *Anaesth Intensive Care* 1993;21:409–413.

9.   Carmichael FJ, Cruise CJ, Crago RR, et al. Preoxygenation: a study of denitrogenation. *Anesth Analg* 1989;68:406–409.

10. Chiron B, Laffon M, Ferrandiere M, et al. Standard preoxygenation technique versus two rapid techniques in pregnant patients. *Int J Obstet Anesth* 2004;13:11–14.

11. Dixon BJ, Dixon JB, Carden JR, et al. Preoxygenation is more effective in the 25° head-up position than in the supine position in severely obese patients: a randomized controlled study. *Anesthesiology* 2005;102:1110–1115.

12. Drummond GB, Park GR. Arterial oxygen saturation before intubation of the trachea. An assessment of oxygen techniques. *Br J Anaesth* 1984;56:987–993.

13. Hirsch J, Führer I, Kuhly P, et al. Preoxygenation: a comparison of three different breathing systems. *Br J Anaesth* 2001;87:928–931.

14. Mort TC. Preoxygenation in critically ill patients requiring emergency tracheal intubation. *Crit Care Med* 2005;33:2672–2675.

15. Stock MC, Schisler JQ, McSweeney TD. The $Paco_2$ rate of rise in anesthetized patients with airway obstruction. *J Clin Anesth* 1989;1:328–332.

16. Rusca M, Proietti I, Schnyder P, et al. Prevention of atelectasis formation during induction of general anesthesia. *Anesth Analg* 2003;97:1835–1839.

17. Greene SA, Harvey RC. Airway disease. In: Thurmon JC, Tranquilli WJ, Benson GJ, eds. *Lumb and Jones' veterinary anesthesia.* 3rd ed. Baltimore: The Williams & Wilkins Co, 1996;807–811.

18. Thurmon JC, Tranquilli WJ, Benson GJ, eds. Cesarean section patients. In: Thurmon JC, Tranquilli WJ, Benson GJ, eds. *Lumb and Jones' veterinary anesthesia.* 3rd ed. Baltimore: The Williams & Wilkins Co, 1996;818–828.

19. Hardman JG, Wills JS, Aitkenhead AR. Factors determining the onset and course of hypoxemia during apnea: an investigation using physiological modeling. *Anesth Analg* 2000;90:619–624.

20. Damia G, Mascheroni D, Croci M, et al. Perioperative changes in functional residual capacity in morbidly obese patients. *Br J Anaesth* 1988;60:574–578.

21. Tusiewicz K, Bryan AC, Froese AB. Contributions of changing rib cage—diaphragm interactions to the ventilatory depression of halothane anesthesia. *Anesthesiology* 1977;47:327–337.

22. Froese AB, Bryan AC. Effects of anesthesia and paralysis on diaphrgamatic mechanics in man. *Anesthesiology* 1974;41:242–255.

23. Drummond GB, Pye DW, Annan FJ, et al. Changes in blood volume distribution between legs and trunk during halothane anaesthesia. *Br J Anaesth* 1995;75:707–712.

24. Nunn JF. Effects of anaesthesia on respiration. *Br J Anaesth* 1990;65:54–62.

25. Drummond GB, Allan PL, Logan MR. Changes in diaphragmatic position in association with induction of anaesthesia. *Br J Anaesth* 1986;58:1246–1251.

26. von Ungern-Sternberg BS, Frei FJ, Hammer J, et al. Impact of depth of propofol anaesthesia on functional residual capacity and ventilation distribution in healthy preschool children. *Br J Anaesth* 2007;98:503–508.

27. Shulman D, Beardsmore CS, Aronson HB, et al. The effect of ketamine on the functional residual capacity in young children. *Anesthesiology* 1985;62:551–556.

28. Smith JA, Gaynor JS, Bednarski RM, et al. Adverse effects of administration of propofol with various preanesthetic regimens in dogs. *J Am Vet Med Assoc* 1993;202:1111–1115.

29. Ogilvie GK, Salman MD, Kesel ML, et al. Effect of anesthesia and surgery on energy expenditure determined by indirect calorimetry in dogs with malignant and nonmalignant conditions. *Am J Vet Res* 1996;57:1321–1326.

30. Proulx J. Respiratory monitoring: arterial blood gas analysis, pulse oximetry and end-tidal carbon dioxide analysis. *Clin Tech Small Anim Pract* 1999;14:227–230.

31. Brandt L. The apnea-$Paco_2$ relationship—unanswered questions? *J Clin Anesth* 1991;3:82–84.

32. Sinex JE. Pulse oximetry: principles and limitations. *Am J Emerg Med* 1999;17:59–67.

33. Wilson WC, Benumof JL. Respiratory physiology. Respiratory physiology and respiratory function during anesthesia. In: Miller RD, ed. *Miller's anesthesia.* 6th ed. St Louis: Elsevier, 2005;679–722.

34. Agarwal A, Singh PK, Dhiraj S, et al. Oxygen in air (Fio_2 0.4) improves gas exchange in young healthy patients during general anesthesia. *Can J Anaesth* 2002;49:1040–1043.