

# Evaluation of oxygen administration with a high-flow nasal cannula to clinically normal dogs

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## OBJECTIVE

To evaluate the safety and efficacy of oxygen administration by use of a high-flow nasal cannula (HFNC) in sedated clinically normal dogs.

## ANIMALS

6 healthy adult dogs undergoing routine dental prophylaxis.

## PROCEDURES

Dogs were sedated with butorphanol tartrate and dexmedetomidine. An esophageal balloon catheter was inserted into the esophagus, a double-pronged nasal cannula was inserted into the nares, and a catheter was inserted into the dorsal pedal artery. Dogs were positioned in right lateral recumbency. After a 6-minute acclimation period, baseline blood gas values and transpulmonary pressure were measured. Dogs then received supplemental oxygen via conventional oxygen therapy (COT) at a rate of 100 mL/kg/min (COT-100 treatment) and an HFNC at a rate of 20 L/min (HF-20 treatment) and 30 L/min (HF-30 treatment). Arterial blood gas and transpulmonary pressure were measured after a 6-minute acclimation period for each oxygen delivery method. Radiographs were obtained before and after oxygen administration to evaluate gastric distension.

## RESULTS

Median  $P_{aO_2}$  was significantly higher for HF-20 (519.9 mm Hg) and HF-30 (538.1 mm Hg) treatments, compared with median  $P_{aO_2}$  for the COT-100 treatment (202.9 mm Hg). The  $P_{aO_2}$  did not differ significantly between the HF-20 and HF-30 treatments. There was no significant difference in  $P_{aCO_2}$  or change in transpulmonary pressure between baseline and any oxygen delivery method.

## CONCLUSIONS AND CLINICAL RELEVANCE

In this study, HFNC appeared to be a safe and effective method for oxygen delivery to sedated healthy dogs. Further studies are needed to evaluate use of HFNCs for oxygen administration to hypoxemic patients. (*Am J Vet Res* 2017;78:624–630)

Respiratory distress is a common problem in veterinary medicine. Regardless of the cause, treatment of respiratory distress includes the provision of supplemental oxygen. Conventional oxygen therapy provided by use of a mask, nasal cannula, hood, or oxygen cage is a noninvasive method that is readily available at most emergency clinics. The  $F_{iO_2}$  supplied to veterinary patients by use of COT is variable, depending on the oxygen delivery device, and is reportedly between 30% and 80%.<sup>1,2</sup> In addition to the fact there is variable  $F_{iO_2}$ , other challenges with COT include lack of patient tolerance with oxygen administered via a mask, inability to monitor  $F_{iO_2}$  with oxygen administered via hoods and cannulas, and limited access to patients in an oxygen cage. Despite these limitations, COT is readily

available at most clinics, can be easily administered, and often is effective for improving hypoxemia.

When use of COT fails to improve hypoxemia, hypercapnia, or work of breathing, more advanced oxygen delivery methods are warranted. Mechanical ventilation has been used in veterinary medicine for advanced management of patients with life-threatening hypoxemia that is unresponsive to COT. Mechanical ventilation requires intubation, a highly sedated or anesthetized patient, expensive equipment, and specialized expertise for operation, and it is labor intensive and is expensive for clients. Although mechanical ventilation is effective for treating hypoxemia, it is associated with complications, including ventilator-associated pneumonia, ventilator-induced lung injury, pneumothorax, tracheal tube occlusion, and gastric distension.<sup>3,4</sup> For dogs and cats receiving mechanical ventilation for pulmonary disease, there is a guarded prognosis, with only 20% to 33% of patients able to be successfully weaned from the ventilator.<sup>3–6</sup> Because of a guarded prognosis, high costs, and complications associated with mechanical venti-

## ABBREVIATIONS

COT	Conventional oxygen therapy
CPAP	Continuous positive airway pressure
$F_{iO_2}$	Fraction of inspired oxygen
HFNC	High-flow nasal cannula
NIV	Noninvasive ventilation

lation, it is understandable why many owners elect for euthanasia of their pets when COT fails and mechanical ventilation is recommended as escalation of treatment.

Noninvasive ventilation, which does not require intubation, has been used in human medicine for decades as an effective advanced method for oxygen delivery. Noninvasive ventilation is used to decrease the work of breathing and improve gas exchange when COT fails.<sup>7,8</sup> Continuous positive airway pressure delivered via a face mask and noninvasive positive-pressure ventilation delivered via a face mask or nasal mask are 2 NIV methods used in humans when COT has failed.<sup>7-9</sup> Clinical use of CPAP and NIV masks has been investigated in dogs and cats.<sup>10-12</sup> These studies have revealed that CPAP and NIV are effective for improving  $P_{aO_2}$ ; however, the degree of sedation required so that a tight mask seal can be maintained for pressure support is high and often to a degree that requires intubation.<sup>10,12</sup> Although effective for improving  $P_{aO_2}$ , the high degree of sedation required to administer oxygen via CPAP or NIV to dogs and cats makes these methods of NIV impractical for veterinary patients.

High-flow nasal cannulas have been used in human medicine since the early 2000s as an NIV method to support hypoxemic patients without the need for intubation. High-flow nasal cannulas were first used in infants and neonates and have since been used for failures of COT, anesthetic recoveries, chronic pulmonary disorders, heart failure, and infants with incomplete alveolar development and in attempts to avoid progression to mechanical ventilation.<sup>9,13,14</sup> In addition, HFNCs have been evaluated for use in humans as a step between COT and mechanical ventilation and as a noninvasive oxygen treatment in do-not-intubate patients.<sup>8,13-17</sup>

Use of HFNCs involves administration of medical-grade, vapor-humidified, heated gas, which allows for high flow rates of up to 60 L/min.<sup>9,13,14,17,18</sup> Nasal administration of oxygen historically has been limited by oxygen flowmeter rates as well as products that can be administered without causing damage to the nasal mucosa. Conventional oxygen therapy involves administration of gases that are not humidified or that are partially humidified through an oxygen bubble humidifier, which can result in inadequate humidification at high flow rates.<sup>18</sup> Inadequate humidification of oxygen for nasal administration causes desiccation of the nasal mucosa and patient discomfort, and it reportedly is associated with staphylococcal sepsis in neonates.<sup>19</sup> In humans, a minimum of 50% relative humidity is recommended for flow rates > 6 L/min.<sup>17</sup> Properly humidified and heated gas allows for the safe delivery of higher oxygen flow rates. Higher oxygen flow rates allow for purging of the respiratory dead space, which eliminates mixing of gases and allows the desired  $F_{iO_2}$  to reach the alveoli.<sup>8,9,13,15,18,20,21</sup>

To the authors' knowledge, safety and efficacy for the use of HFNCs have not been evaluated in vet-

erinary patients. The objective of the study reported here was to evaluate the safety and efficacy of use of an HFNC in a group of healthy dogs. The 2 primary hypotheses for this study were that the  $P_{aO_2}$  would be higher with use of an HFNC, as compared with COT, and that high flow rates of oxygen could be safely administered to a population of healthy dogs, as determined by measurement of transpulmonary pressure and monitoring of gastric distension.

## Materials and Methods

### Animals

Six healthy client-owned dogs undergoing routine dental prophylaxis were included in the study. The study group consisted of 1 Labrador Retriever, 1 pit bull-type dog, 1 German Shepherd Dog, and 3 mixed-breed dogs. Mean body weight of the dogs was 28 kg (range, 17 to 36 kg), and mean age was 4.8 years (range, 3 to 9 years). All dogs were deemed healthy prior to the study on the basis of results of a physical examination, blood biochemical analysis, CBC, and urinalysis. Owner consent was obtained for inclusion of each dog. The study was approved by the Clinical Studies and Trials Committee of Pittsburgh Veterinary Specialty and Emergency Center.

### Experimental procedures

Each dog was sedated by IV administration of butorphanol tartrate<sup>a</sup> (0.2 mg/kg) and dexmedetomidine<sup>b</sup> (3  $\mu$ g/kg). An 18-gauge over-the-wire catheter<sup>c</sup> was inserted into a cephalic vein, a 22-gauge over-the-wire catheter<sup>c</sup> was inserted into a dorsal pedal artery, and a double-prong nasal cannula<sup>d</sup> was inserted into the nares. Size of nasal cannulas was selected such that the diameter of the nasal prong was approximately 50% of the diameter of the nares. Transpulmonary pressure was obtained as described elsewhere.<sup>22</sup> Briefly, an esophageal balloon catheter was inserted into the esophagus, with placement of the balloon determined by measuring the distance from the mandibular incisors to the head of the 10th rib and subtracting 5 cm.<sup>22</sup> A right lateral radiograph was then obtained and used for baseline gastric measurements and to ensure proper placement of the esophageal balloon catheter.

Dogs were positioned in right lateral recumbency to induce mild hypoxemia, as described elsewhere.<sup>23,24</sup> The esophageal balloon catheter was connected to a portable veterinary monitoring device<sup>e</sup> for pressure monitoring. Pressures were calibrated to 0 mm Hg. After each dog had a 6-minute acclimation period,<sup>1,23,24</sup> a blood sample was collected from the catheter in the dorsal pedal artery into a blood gas syringe<sup>f</sup>; a baseline arterial blood gas value was immediately obtained by use of a commercial blood analyzer.<sup>8</sup> Baseline transpulmonary pressures were then recorded at the end of expiration.

Each dog then received supplemental oxygen via each of 3 methods. Dogs were randomly assigned via a block randomization method to receive oxygen via

HFNC at a rate of 20 L/min (HF-20 treatment), HFNC at a rate of 30 L/min (HF-30 treatment), and COT at a rate of 100 mL/kg/min (COT-100 treatment). A commercially available HFNC unit<sup>b</sup> was used for HF-20 and HF-30 treatments. Settings for the HFNC unit were an  $F_{iO_2}$  of 100%, gas temperature of 38°C, and gas flow rate of 20 or 30 L/min. For the COT treatment, a standard wall oxygen bubble humidifier was used, and the flow rate was calculated for each dog on the basis of body weight.

During the study period, heart rate, respiratory rate, and oxygen saturation measured by use of pulse oximetry were monitored continuously, and blood pressure and rectal temperature were recorded every 5 minutes with a clinical vital signs monitor.<sup>c</sup> Dogs received oxygen via each method for an acclimation period of  $\geq 6$  minutes before sample data were collected. After the end of the 6-minute acclimation period for each oxygen delivery method, an arterial blood sample was collected and blood gas values were determined. Transpulmonary pressures were recorded at the end of expiration. After the data collection, dogs immediately received oxygen via the next method.

A right lateral radiograph of each dog was obtained at the end of the study period and used to evaluate the development of gastric distension. The radiographs obtained before and after the study were reviewed by a board-certified veterinary radiologist, who was unaware of the order in which the radiographs were obtained.

After data collection for the study was completed for all oxygen delivery methods, all dogs were tracheally intubated. Anesthesia was induced and maintained by administration of isoflurane, and dental prophylaxis procedures were performed.

## Statistical analysis

Statistical analysis was performed by use of standard statistical software.<sup>1</sup> Descriptive statistics (median, mean, and SD) were calculated for the blood gas variables  $P_{aO_2}$  and  $P_{aCO_2}$  and the change in transpulmonary pressure from the baseline value. The sample

size for the study ( $n = 6$ ) was small, and data were not normally distributed. The Friedman rank sum test (a nonparametric ANOVA) was used for comparison of variables among methods. Post hoc analysis was performed by use of Wilcoxon signed rank tests for paired data to compare variables between baseline and the various oxygen administration methods. A Benjamini-Hochberg correction was applied to all tests to adjust for multiple comparisons. Correlations were calculated by use of the Spearman correlation coefficient. For all analyses, results were considered significant at  $P < 0.05$ .

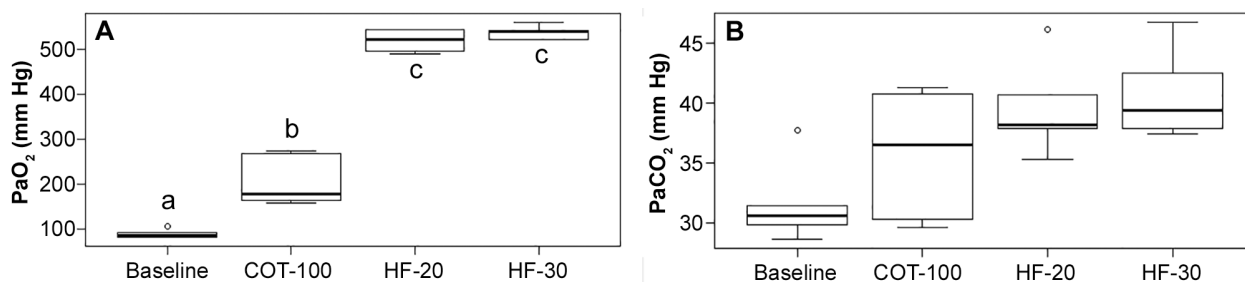
## Results

Baseline (ie, before administration of supplemental oxygen) median  $P_{aO_2}$  was 85.9 mm Hg (range, 81.1 to 105.7 mm Hg). All oxygen delivery methods resulted in a significant improvement in  $P_{aO_2}$  from the baseline value (**Figure 1**). In addition, median  $P_{aO_2}$  for the HF-20 (519.9 mm Hg; range, 490.3 to 545.0 mm Hg) and HF-30 (538.1 mm Hg; range, 522.0 to 560.9 mm Hg) treatments was significantly ( $P = 0.038$ ) higher than the median  $P_{aO_2}$  for the COT-100 treatment (202.9 mm Hg; range, 158.1 to 273.2 mm Hg). Values for  $P_{aO_2}$  did not differ significantly ( $P = 0.313$ ) between the HF-20 and HF-30 treatments.

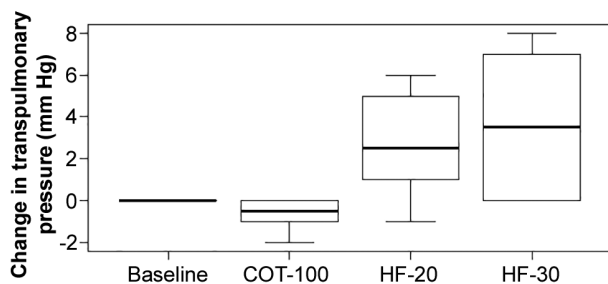
The  $P_{aCO_2}$  did not differ from the baseline value for any oxygen delivery method (Figure 1). There was a pattern whereby  $P_{aCO_2}$  increased with higher flow rates; however, none of the differences in  $P_{aCO_2}$  were significant, and all  $P_{aCO_2}$  values were within reference limits of dogs for the analyzer used.

Transpulmonary pressure did not differ significantly between the baseline value and any oxygen delivery method (**Figure 2**). In addition, there was no significant difference in transpulmonary pressure between the COT-100 treatment and the HF-20 or HF-30 treatments.

None of the dogs had complications during or after the study. One dog had radiographic evidence of gastric distension at completion of the study. However, the gastric distension was not clinically apparent, and the dog did not require medical intervention.



**Figure 1**—Box-and-whisker plots of  $P_{aO_2}$  (A) and  $P_{aCO_2}$  (B) values obtained for 6 sedated healthy dogs before (baseline) and after oxygen administration via COT at a rate of 100 mL/kg/min (COT-100 treatment) and HFNC at a rate of 20 L/min (HF-20 treatment) and 30 L/min (HF-30 treatment). Each box represents the second and third quartiles, the bar in each box represents the median, whiskers represent the first and fourth quartiles, and circles represent outliers. Dogs were allowed a 6-minute acclimation period for baseline and each oxygen delivery method before data collection. Notice the pattern whereby  $P_{aCO_2}$  increased with higher flow rates; however, differences in  $P_{aCO_2}$  were not significant, and all  $P_{aCO_2}$  values were within reference limits of dogs for the analyzer used. <sup>a-c</sup>Values with different letters differ significantly ( $P < 0.05$ ).



**Figure 2**—Box-and-whisker plot of the change in transpulmonary pressure for 6 sedated healthy dogs before (baseline) and after oxygen administration via each of 3 oxygen delivery methods. See Figure 1 for key.

## Discussion

The study reported here was, to the authors' knowledge, the first in which safety and efficacy for use of HFNC in dogs has been described. Use of an HFNC significantly improved  $P_{aO_2}$ , compared with results for COT. When COT fails to improve hypoxemia and work of breathing, more advanced oxygen delivery methods are indicated. In humans in which COT fails, several advanced oxygen delivery options are available that do not require intubation. The CPAP and other NIV methods involve the use of face masks or nasal masks and are successful for improving respiratory variables in humans in which COT has failed.<sup>8,13,25</sup> Unfortunately, CPAP and other NIV methods of oxygen delivery, although effective for relieving hypoxemia in veterinary patients, have not proven to be practical in a clinical setting.<sup>10-12</sup> Thus, advanced oxygen delivery methods when COTs have failed in veterinary patients have been historically limited to invasive methods of oxygen delivery that require intubation. Positive-pressure ventilation is 1 such method of oxygen delivery, and although it is successful for improving hypoxemia in veterinary patients, it is associated with high morbidity and mortality rates and is labor intensive and expensive.<sup>3,4</sup> Because of the lack of advanced noninvasive oxygen delivery methods available in veterinary medicine, an HFNC was investigated as a potential method to avoid intubation during escalation of oxygen administration to dogs for which COT failed.

High-flow nasal cannulas have been used in human medicine for > 15 years as a method of escalation of oxygen treatment for humans in which COT has failed.<sup>8,15,26</sup> Reported advantages of HFNC over COT for humans include less work of breathing, dead-space washout, less metabolic work associated with gas conditioning, a mild distending pressure, delivery of a consistent  $F_{IO_2}$ , improved mobilization of secretions, and improved pulmonary conductance, compliance, and lung elasticity.<sup>8,14,15,17,25,26</sup> When HFNC methods are compared with CPAP and other NIV methods, there have been similar clinical outcomes for avoiding intubation.<sup>8,13</sup> However, in 1 study,<sup>8</sup> there were more ventilator-free days and an improved 90-day outcome with HFNC, compared with results for NIV,

in people with acute hypoxemic respiratory failure. People receiving treatment by use of an HFNC report more comfort, compared with results for use of CPAP and NIV, primarily because HFNCs do not require a tight-fitting mask.<sup>15,21</sup> People receiving oxygen by use of an HFNC are able to eat, drink, and talk during treatment and therefore are less likely to discontinue administration of supplemental oxygen.<sup>8,15,26</sup> Adverse effects with the use of HFNCs in human patients are not common and include air leak syndromes (pneumothorax and pneumomediastinum) as well as cervicothoracic and nasal discomfort.<sup>26-29</sup> The efficacy and benefits of use of HFNC methods over CPAP and other NIV methods for humans are still being debated.<sup>8,13,17,30</sup>

In the study reported here, calculated minute ventilation was exceeded for all dogs at flow rates of 20 and 30 L/min but was not exceeded with COT at a rate of 100 mL/kg/min (data not shown). On the basis of results for humans, it is likely that improvements in  $P_{aO_2}$  with HF-20 and HF-30 treatments were secondary to dead-space washout from higher inspiratory flow rates.<sup>31</sup> Anatomic dead-space washout occurs with higher flow rates of gas and has been implicated as the major reason for improvements in  $P_{aO_2}$  seen with use of HFNCs.<sup>8,13,32</sup> When inspiratory flow rates are calculated to exceed minute ventilation, purging of the respiratory dead space can occur. Minute ventilation is equal to tidal volume multiplied by respiratory rate, whereby estimated tidal volume in dogs is 10 to 20 mL/kg.<sup>33</sup> In 1 study,<sup>31</sup> increasing the flow rates increased  $P_{aO_2}$  in a flow-dependent manner until saturation was reached. At saturation, complete dead-space wash out was proposed to have been achieved and increases in  $P_{aO_2}$  were no longer evident.<sup>31</sup> When complete dead-space washout is achieved, the alveoli are filled with freshly oxygenated gas that does not contain residual expiratory gas with  $CO_2$  from the anatomic dead space. Thus, the alveoli are able to receive the desired  $F_{IO_2}$  because there is no admixture of end-expiratory gases, which allows for improved alveolar ventilation with decreased minute ventilation and decreased work of breathing.

Another objective for the study reported here was to assess the safety for high gas flow rates by measuring changes in transpulmonary pressure. In the present study, change in transpulmonary pressure was measured by use of an esophageal balloon catheter. Direct measures of thoracic pressures are more accurate than the indirect measure used in this study. Thoracic pressures can be measured by use of a pleural transducer (the criterion-referenced standard) or tracheal catheters.<sup>34-36</sup> However, esophageal pressure can be used as a measure of pleural or transpulmonary pressure. Esophageal pressure measurement is a less invasive method for monitoring changes in pressure and can be an acceptable alternative method for use in human and canine patients.<sup>22,35,36</sup> Although the high flow rates exceeded the calculated minute ventilation in all dogs in the present study, there was

no significant change in transpulmonary pressures detected at any point in the study.

In the present study, nasal cannulas were fitted to the dogs so that the nasal prongs did not exceed > 50% of the diameter of the nares, per manufacturer recommendations. This recommendation resulted in a high-leak cannula that allowed the dogs to easily exhale past the nasal prongs. Use of such high-leak cannulas in studies with adult<sup>37</sup> and neonatal<sup>38</sup> humans allowed for improved dead-space clearance and reduction in unintended pressure generation. Although HFNCs are not intended to be used to provide pressure support, a pressure effect has been associated with use of HFNCs in humans. There was an increase in positive end-expiratory pressure (0.69 cm H<sub>2</sub>O for every 10 L of flow/min) during closed-mouth administration via an HFNC in healthy adults.<sup>18,21</sup> However, lower nasopharyngeal pressures with open-mouth administration via an HFNC, compared with pressures for closed-mouth administration, have been reported for humans in other studies.<sup>21,30</sup> Studies<sup>39,40</sup> conducted with human neonates by use of flow rates from 1 to 6 L/min have confirmed that pressures were similar to those for CPAP at 6 cm H<sub>2</sub>O. Conversely, in a study<sup>31</sup> of neonatal pigs with experimentally induced acute respiratory distress syndrome, no significant elevation of thoracic pressure was found with any of the tested flow rates. Despite increases in end-expiratory pressure in people receiving oxygen treatment by use of an HFNC, a significant change in end-expiratory pressure was not detected in the dogs reported here. This may have been attributable to the small number of dogs in the study. Whether the study dogs were breathing with an open or closed mouth during the study period was not recorded; therefore, the impact of that factor on transpulmonary pressure could not be evaluated.

The HFNC used in the present study created a medical-grade vapor-humidified gas by passing the air through a specialized membrane.<sup>41</sup> Heated and humidified air purportedly results in less damage to the nasal mucosa, improves patient comfort, and improves pulmonary compliance and conductance.<sup>17</sup> This is thought to be a primary reason for improved patient compliance and a reduction in treatment failure, compared with outcomes for CPAP and NIV methods. Intolerance and patient discomfort leading to treatment interruption with NIV methods have been reported for humans.<sup>17,39</sup> In veterinary medicine, higher flow rates of gas (flow rates > 100 mL/kg/min) can cause patient discomfort.<sup>1</sup> Adverse effects with the use of HFNCs in human patients are not common and include air leak syndromes (pneumothorax and pneumomediastinum) as well as cervicothoracic and nasal discomfort.<sup>17,26,27</sup> In the present study, the dogs were sedated to facilitate placement of esophageal balloon catheters; thus, patient tolerance of an HFNC could not be evaluated, although none of the dogs developed any form of air leak syndrome.

Gastric distension has been reported as a consequence for several methods of oxygen administration to humans. Although rare, gastric rupture secondary to gastric distension with oxygen administered by use of an intratracheal catheter has been reported,<sup>42-44</sup> and CPAP users have reported discomfort attributable to aerophagia.<sup>45,46</sup> Gastric distension has not been reported as a complication with HFNC use in adults and neonates.<sup>43</sup> Gastric distension was not evaluated in an evaluation of CPAP use in dogs,<sup>10</sup> nor was it found during evaluation of the use of NIV in cats.<sup>12</sup> One of 6 dogs in the present study had radiographic evidence of gastric distension at completion of the study, but it was not clinically relevant, and no interventions were required. Patients receiving oxygen by use of an HFNC should be monitored for signs of gastric distension (eg, abdominal discomfort and abdominal distension).

Use of fresh gas to purge anatomic dead space results in a decrease in rebreathing of end-expiratory air high in CO<sub>2</sub>. Because of this function, HFNCs have been used in patients with hypercapnia.<sup>47</sup> One study<sup>31</sup> included 2 patient populations (use of low-leak and high-leak HFNCs in neonatal pigs with induced acute respiratory distress syndrome). Results of that study<sup>31</sup> indicated a sigmoidal decrease in PaCO<sub>2</sub> for the low-leak conditions and immediate return to baseline values for the high-leak conditions. Dead-space washout that occurs with use of HFNCs is considered another benefit, with decreased minute ventilation and work of breathing.<sup>15,31</sup> Although there was a pattern of an increase in PaCO<sub>2</sub> at higher flow rates in the study reported here, the change was not significant, and PaCO<sub>2</sub> remained within reference ranges for all dogs during the study. Possible considerations for the increase in PaCO<sub>2</sub> in this population of dogs would include mild hypoventilation attributable to the degree of sedation and air trapping secondary to the high oxygen flow rates, which caused a CPAP effect. Additional studies will be needed to evaluate PaCO<sub>2</sub> in hypoxemic dogs receiving oxygen by use of an HFNC.

The purpose of the present study was to prove efficacy and safety for the use of an HFNC in dogs. To determine the effect of higher gas flow rates on pulmonary pressures, dogs in the study were heavily sedated to enable placement of an esophageal balloon catheter. Because of the degree of sedation required, patient tolerance could not be evaluated for changes in oxygen flow rates. Patient tolerance with CPAP and NIV by use of a face mask can be a major complication in dogs and cats, which makes use of a CPAP for oxygen delivery clinically unfeasible for veterinary patients unless they are heavily sedated.<sup>10-12</sup> Further studies are needed to evaluate patient tolerance for use of HFNCs in nonsedated dogs.

In the present study, use of an HFNC significantly improved Pao<sub>2</sub>, compared with results after oxygen administration via a nasal cannula at a rate of 100 mL/kg/min. Adequately humidified and heated oxy-

gen administered at flow rates of 20 and 30 L/min appeared to be a safe method of oxygen administration, with minimal complications in healthy dogs with no abnormalities of pulmonary function. Further studies are needed to evaluate efficacy and patient tolerance for use of HFNCs in awake dogs with abnormal pulmonary function.

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## Footnotes

- a. Merck, Whitehouse Station, NJ.
- b. Zoetis, Parsippany, NJ.
- c. Sureflo, Terumo Medical Corp, Elkton, Md.
- d. High-flow therapy nasal cannula, Vapotherm Inc, Exeter, NH.
- e. Advisor vital signs monitor, Smith Medical, Dublin, Ohio.
- f. Line draw, 1 mL, Smiths Medical, Keene, NH.
- g. Nova pHOX Ultra, Nova Biomedical Corp, Waltham, Mass.
- h. Vapotherm Precision Flow, Vapotherm Inc, Exeter, NH.
- i. R Core Team (2014), R Foundation for Statistical Computing, Vienna, Austria. Available at: [www.r-project.org/](http://www.r-project.org/). Accessed Aug 9, 2014.

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