Prospective pilot study for evaluation of high-flow oxygen therapy in dyspnoeic dogs: the HOT-DOG study

Céline Pouzot Pouzot-Névoret, L Hocine, J Nègre, Isabelle Goy-Thollot, Anthony Barthélemy, E Boselli, Jeanne-Marie Bonnet-Garin, B Allaouchiche

Prospective pilot study for evaluation of High-flow Oxygen Therapy in dyspneic dogs: the HOT-DOG study

C. Pouzot-Nevoret[1,2], DV, PhD, Dipl ECVECC, L. Hocine[1,2], **DV, MSc,** J. Nègre[2,3], PT, I. Goy-Thollot[1,2], DV, PhD, Dipl ECVECC, A. Barthélémy[1,2], DV, PhD, E. Boselli[2], MD, PhD, J.M. Bonnet[2], DV, PhD, B. Allaouchiche[2,3], MD, PhD

[1] Intensive Care Unit (SIAMU), Université de Lyon, VetAgro Sup, APCSe, F-69280, Marcy l'Etoile, France

[2] Université de Lyon, VetAgro Sup, APCSe, F-69280, Marcy l'Étoile, France

[3] Hospices Civils de Lyon, Centre Hospitalier Lyon-Sud, Service de Réanimation, F-69310, Pierre-Bénite, France

Corresponding author: Céline Pouzot-Nevoret DVM, MS, PhD, Intensive Care Unit (SIAMU), VetAgro Sup, Campus Vétérinaire de Lyon, 1 avenue Bourgelat, 69280 Marcy l'Étoile, France

Cell: +336 82 74 34 05

Email: celine.pouzotnevoret@vetagro-sup.fr

No conflicts of interest have been declared.

Keywords: Hypoxemia, High-flow oxygen therapy, Dyspnoea, Mechanical Ventilation, Nasal cannula

Acknowledgment

The authors would like to thank Dr Mathieu Taroni for the realisation of the Figure 1.

Abstract

Objectives: To describe the use, effectiveness and tolerance of high-flow oxygen therapy in dyspneic dog.

Methods: Prospectively, dogs in acute respiratory distress admitted to the ICU between January and May 2018 that failed to respond to nasal oxygen therapy and medical stabilization after 30 minutes were transitioned to high-flow oxygen therapy and included in the study. High-flow oxygen therapy, delivering an inspired oxygen fraction of 100%, was carried out using an air/oxygen blender, active humidifier, single heated tube, and specific nasal cannula. Respiratory rate (RR), pulse oxymetry ($SpO_{2)}$, heart rate (HR), and tolerance score were assessed every 15 minutes from T_0 (under nasal oxygen) to 1 hour (T_{60}), and PaO_2 and $PaCO_2$ at T_0 and T_{60}. Complications were recorded for each dog.

Results: Eleven dogs were included. At T_{60}, PaO_2, flow rate, and SpO_2 were significantly greater than at T_0 (171 ±123 mmHg *vs* 73 ±24 mmHg; P=0.015; 18 ±12 L minute^{-1} *vs* 3.2 ±2.0 L minute^{-1}, P<0.01; 97.7 ±2.3% *vs* 91.6 ±7.2%, P=0.03, respectively). There was no significant difference in $PaCO_2$, RR, HR between T_0 and T_{60}. Tolerance score was excellent, and no complication occurred.

Clinical significance: This study established that high-flow oxygen therapy improves markers of oxygenation in dyspneic dogs and confirms that this technique deliver effective oxygen with comfort and minimal complications in this population.

Introduction

Supplemental oxygen administration is the first supportive measure provided to dyspneic dogs upon admission to an emergency facility. In veterinary medicine, oxygen therapy is mostly delivered by non-invasive techniques such as flow-by, nasal prongs, or oxygen cages. These methods are known as conventional oxygen therapy (COT) and can achieve variable fractions of inspired oxygen (FIO_2) ranging from 21 to 70% (Sumner & Rozanski 2013). When patients remain hypoxemic despite COT, clinicians may choose among more advanced oxygen delivery methods. One option is mechanical ventilation, which however requires prolonged general anaesthesia, continuous advanced care and is associated with frequent complications, high costs, and, depending on the underlying disease, a guarded prognosis - often leading the owner to a decision of euthanasia (Hopper *et al.* 2007, Mueller 2007). In human medicine, non-invasive ventilation (NIV) is a popular method to avoid intubation. Continuous positive airway pressure (CPAP) is a NIV mode that has been validated in dogs (Briganti *et al.* 2010, Staffieri *et al.* 2014, Meira *et al.* 2018). Continuous positive airway pressure is effective to improve arterial partial pressure of oxygen (PaO_2) in companion animals when used with devices such as masks or helmets (Briganti *et al.* 2010, Staffieri *et al.* 2014, Meira *et al.* 2018) and can be used in dyspneic animals.

In human medicine, a non-invasive oxygen delivery technique known as high-flow oxygen therapy (HOT) has emerged as an alternative to COT (Helviz *et al.* 2018). This system allows for delivery of heated and fully humidified gas with high flow rates of up to 60 L $minute^{-1}$ through a specific high-flow nasal cannula, with a FIO_2 ranging from 21% to 100% (Frat *et al.* 2015). Such high flow rates are not achievable with COT because of technical limitations (flowmeters rates, diameter of the nasal prongs). Furthermore, administration of a partially humidified, cold gas could cause patient discomfort, desiccation of the nasal mucosa, airway constriction, impairment

of the mucociliary functions, and increased risk of infection if delivered at similar rates (Kallstrom 2002, Dunphy *et al.* 2004, Kilgour *et al.* 2004, Kopelman & Holbert 2003).

High-flow oxygen therapy uses an air-oxygen blender connected to a flow meter, an active humidifier and heater, a heated breathing circuit, and a specific nasal cannula (Nishimura 2016) (Figure 1). Warm and adequately humidified gas delivered at high flow rates has apparent beneficial physiological effects that are increasingly recognized in humans. These include: good tolerance (Sztrymf *et al.* 2012) and comfort (Roca *et al.* 2010, Frat *et al.* 2015), decreased mismatch between the oxygen flow and the patient's inspiratory flow (Sztrymf *et al.* 2012), allowing precise setting by the clinician; generation of a low level of positive airway pressure (Groves & Tobin 2007, Parke *et al.* 2011), decreased anatomical dead space by washing the expired volume of carbon dioxide from the airway and replacing it with oxygen-enriched gas (Helviz *et al.* 2018, Hernández *et al.* 2017, Millar *et al.* 2014), and decreased ventilatory drive and work of breathing in obstructive human patients (Di Mussi *et al.* 2018), allowing the use of HOT in hypoxemic and hypercapnic respiratory failure.

High flow oxygen therapy has recently been studied in veterinary medicine. It has been shown to be a safe and effective method for oxygen delivery in sedated and awake healthy dogs (Daly *et al.* 2017; Jagodich *et al.* 2019), and a preliminary retrospective study described its successful use in six hypoxemic dogs (Keir *et al.* 2016). No prospective study reporting the use of HOT in dyspneic dogs has been conducted. The objective of this pilot study was to prospectively describe the use, tolerance and potential complications of HOT in dyspneic dogs.

Materials and Methods

Ethical statement

The study protocol was approved by the VetAgro Sup Ethics committee (number 1730).

Animals

This prospective pilot study was conducted between January and May 2018 in the emergency and critical care unit (SIAMU, VetAgro Sup) on client-owned dogs admitted for acute respiratory distress. Respiratory distress at admission was defined as a respiratory rate (RR) above 40 breaths minute^{-1} associated with an abnormal respiratory pattern or laboured breathing at rest.

Inclusion

After admission, all respiratory distressed patients received 100% oxygen delivered via a single nasal cannula at 150 mL kg^{-1} minute^{-1} (Dunphy *et al*. 2002, Mazzaferro 2015), using a standard wall water humidifier (COT). Standard therapy for stabilization of the respiratory distress was administered based on the most likely diagnosis, at the discretion of the attending clinician, independently from the study. After 30 minutes of medical stabilization, dogs non-responsive to nasal oxygen therapy were transitioned to HOT and prospectively enrolled in the study. Dogs non-responsive to nasal oxygen therapy (inclusion criteria) were defined as persisting respiratory distress as previously defined or a SpO_2<95% under nasal oxygen at the end of the 30-minute stabilization period. Owner consent was obtained prior to transition from nasal oxygen therapy to HOT.

Exclusion criteria

The exclusion criteria were a body weight below 2 kg, adequate response to COT defined as respiratory distress improvement and SpO_2>95%, or criteria for immediate intubation, defined as excessive respiratory effort with impending respiratory fatigue or failure, severe hypoxemia despite oxygen therapy (SpO_2<90% or PaO_2<60 mmHg), or a severe hypercapnia (arterial partial pressure of carbon dioxide ($PaCO_2$)>60 mmHg).

Early termination criteria were failure to tolerate HOT (defined by a tolerance score (TS) equal to 4, Table 1) and fulfilment intubation criteria (as defined above). Dogs with a do-not-intubate order remained on HOT despite being intubation candidates.

High-flow oxygen technique description

High flow oxygen therapy was delivered by a commercially available unit connected to a specific nasal cannula interface (Optiflow®, Fisher&Paykel Healthcare). The system is composed of an air-oxygen blender connected to oxygen wall source, a flow meter, an active humidifier and heater, a heated breathing circuit, and a specific nasal cannula (Figure 1). The nasal cannula is a soft silicone bilateral nasal prong with tubing that connects to the heated breathing circuit (Figure 2). The system allows for administration of humidified and warmed gas with a FIO_2 between 21 and 100%. Continuous humidification was ensured by a water chamber connected to a sterile water bag. Temperature was set at 37°C and administered to the patient via the heated breathing tube.

The nasal cannula was chosen according to the size of the dog's nostrils, so that the cannula diameter would not exceed 50% of the diameter of the nostril and therefore allowed exhalation with minimal resistance (Daly *et al.* 2017). Seven different sizes were available (4 junior, 3 adult). Once the size of the nasal cannula was chosen, they were gently tightened behind the neck, and eventually secured with tape and sutured in place next to each nare (Figure 2).

In order to avoid recruitment of oxygen from the surrounding air and assure the delivery of the predetermined FIO_2, the oxygen flow rate was set to be equivalent to the dog's minute ventilation (MV=RR*tidal volume) (Helvis *et al.* 2018). For homogeneity, tidal volume was set at 10 mL kg^{-1} (Grimm *et al.* 2015). For example, a 30 kg dog with a RR of 80 breaths $minute^{-1}$ had a flow rate with HOT of 10*30*80=24 L $minute^{-1}$ (compared to a flow rate of 4.5 L $minute^{-1}$ with nasal oxygen therapy). The FIO_2 was set at 100% and the gas temperature at 37°C during the 60-

minute protocol. Once setting was ready, the patient was connected to the heated breathing tube. At the end of the 60-minute protocol period, the FIO_2 was adjusted to the lowest level possible to maintain SpO_2>95%.

Data recording

The RR, SpO_2, heart rate (HR), TS (Table 1), flow rate, need for additional sedation, type and dose of sedative agent used and complications during HOT were recorded by the same operator (LH). Each of these parameters was recorded right after the 30-minute stabilization period (T_0), when dogs were still receiving nasal oxygen therapy. The oxygen delivery technique was then changed from nasal oxygen therapy to HOT and the parameters were recorded immediately at 15, 30, 45 and 60 minutes after T_0 (T_{15}, T_{30}, T_{45}, and T_{60}, respectively). A catheter was inserted in the dorsal pedal artery to allow drawing of arterial blood samples and evaluate PaO_2 and PCO_2 at T_0 (under nasal oxygen therapy) and T_{60} (under HOT). Arterial blood gases measurements were performed on fresh whole arterial blood collected in a heparinized syringe according to the manufacturer's instructions using an on-site VetStat (IDEXX Laboratories Inc.).

An $APPLE_{fast}$ scale (0-50 score, calculated from glucose, albumin, lactate, platelet count, and mentation score) was used in each dog at inclusion to stratify illness severity by mortality risk as previously described (Hayes *et al.* 2010).

Outcomes

The evolution of PaO_2, $PaCO_2$ and flow rate between T_0 and T_{60}, and evolution of RR, tolerance score, SpO_2 and HR every 15 minutes during the 60-minute protocol were recorded. The occurrence of complications due to the oxygen delivery technique during the protocol, requirement for escalation to intubation within 24 hours after admission and in-hospital mortality were also recorded.

Statistical method

Statistical analyses were carried out with JMP® version 13.1 (SAS institute). All individual data were described with a spaghetti plot graphic. Data were tested for normal distribution with the Shapiro-Wilk test. Continuous variables were compared with paired t-tests. Data were expressed as mean ± standard deviation (SD) with 95% confidence intervals (CI). A value of $P<0.05$ was considered as statistically significant.

Results

Animals

During the study period, 11 dogs were included in the high flow oxygen therapy protocol. The breeds of dogs included were three Golden Retriever, two King Charles Spaniel, two Dachshunds and one each of Australian Shepherd, German Wirehaired Pointer, Jack Russell Terrier and Pomeranian. Four dogs were female neutered and seven were male neutered, with mean ±SD weights of 28.3 ±12.3 kg (range, 4.8 to 43.0 kg) and ages 7.8 ±3.8 years (range, 2 to 13 years).

Five dogs had a diagnosis of aspiration pneumonia, and one of each: cardiogenic pulmonary oedema, non-cardiogenic oedema following cluster seizures, leptospirosis infection, pulmonary haemorrhages following a car accident, pulmonary hypertension of unknown origin, and pericardial effusion. The mean ±SD $APPLE_{fast}$ score was 27.0 ±4.4

Recorded data

Dogs were receiving nasal oxygen therapy at T_0 and HOT at T_{15}, T_{30}, T_{45} and T_{60}.

PaO_2

High-flow oxygen therapy allowed a significant increase in mean PaO_2 at T_{60} (171 ±123 mmHg) compared to nasal oxygen therapy at T_0 (73 ±24 mmHg; P=0.015, 95% CI: 23 to 172 mmHg).

Individual data are presented in Figure 3. For every dog, PaO_2 increased after HOT initiation. Of the 7 dogs with PaO_2<80 mmHg at COT, 5 had a resolution of their hypoxemia one hour after HOT initiation.

Flow rate (Figure 4)

The mean oxygen flow rate was significantly greater with HOT (18 ±12 L minute^{-1}) than in nasal oxygen technique (3.2 ±2.0 L minute^{-1}, P<0.01, 95% CI: 8.0 to 22.5 L minute^{-1}). Flow rate with HOT ranged from 2 to 37 L minute^{-1}. Flow rate with nasal oxygen technique ranged from 0.7 to 6.5 L minute^{-1}.

Respiratory rate

Individual data are presented in Figure 5. Six dogs had a decrease in RR between T_0 and T_{60}. However, only 2 dogs reached our criteria of respiratory distress of less than 40 breaths minute^{-1} at T_{60} despite the use of HOT.

SpO_2, HR and $PaCO_2$

The mean SpO_2 was significantly greater at T_{60} (97.7 ±2.3%) than at T_0 (91.6 ±7.2%, P=0.03, 95% CI: 0.7 to 11.5%). There was no significant difference at any time for HR or $PaCO_2$. All individual data are showed in figure 6, 7, and 8 (supplemental material).

Tolerance score

The TS remained low during the entire protocol. Only one animal displayed a TS of 3 when setting the HOT device, requiring additional sedation that lowered its TS to 2 or 1 depending on the protocol time. Another dog displayed a TS of 2 at two occurrences but did not need any additional sedation. Every other dog had a TS of 1 at every protocol time.

Complications

No complications due to the oxygen delivery technique occurred during the study. Nasal cannulas were easy to fix and to use. No injuries occurred due to the nasal cannula.

Intubation within 24 hours and mortality in hospitalisation

Five of the 11 dogs (45%) developed a need for intubation within 24 hours after admission. Due to financial reasons, only 3 of them (27%) were intubated. Six of 11 dogs (54%, including the 5 that presented intubation criteria) died during hospitalization. Death were due to deteriorating clinical state leading to cardiac arrest in 5 dogs and 1 euthanasia for prognostic reason.

Discussion

This is the first prospective clinical trial evaluating the effectiveness and tolerance of HOT in respiratory distress dogs. Our study shows the potential for HOT to be an efficient, safe and well-tolerated alternative to COT with nasal oxygen therapy to deliver oxygen. This technique allows for a significant increase in PaO_2 in dogs, with the PaO_2 more than doubling between nasal oxygen therapy and HOT within only one hour. This finding is consistent with the human (Sztrymf *et al*. 2012, Frat *et al.* 2015, Makdee *et al.* 2017), and the veterinary literature. Indeed, Daly *et al.* (2017) and Jagodich *et al.* (2019) in healthy dogs, and Keir *et al.* (2016) in hypoxemic dogs showed this PaO_2 improvement after HOT. With such an increase in PaO_2 during a short

period of time, HOT raised concern for oxygen toxicity if continued for a long time. For homogeneity in the study design, the authors chose to keep the FIO_2 up to 100% during the 60-minute protocol, but FIO_2 was decreased immediately at the end of the protocol to the lowest required FIO_2 to reach a SpO_2>95%. As high-flow devices offer multi-configurable solutions for flow and FIO_2, theses two parameters can be changed easily to fit patient's demand. Once the targeted oxygenation parameters are reached and plateaued, the FIO_2 should be decreased under 60% as soon as possible to avoid oxygen toxicity (Guenther 2019).

In the present study, flow rates with HOT ranged from 2 to 37 L $minute^{-1}$ and resulted in an increase in PaO_2 in all cases (Figure 3). By delivering higher flow rates, HOT systems are less prone to allow inhalation of room air during patient inspiration than traditional oxygenation systems (Helvis *et al.* 2018). Different systems exist for high-flow delivery: Precision flow (Vapotherm), Optiflow (Fisher&Paykel Healthcare), Airvo system (Fisher&Paykel Healthcare). Each of them has specific characteristics and has to be used with their specific nasal cannula to ensure appropriate flow rate, temperature, and FIO_2. In our study, we used the Optiflow system which was easy to use and offer a multi-configurable solution for patients requiring HOT. This system relies on an O_2/air blender, and FIO_2 of 100% is obtained with use of oxygen wall not mixed with air. No internal system was available to ensure that the delivered FIO_2 at the nasal cannula was at 100%. We were not able to measure the delivered FIO_2 in our study, and some dogs were panting during measurements, so we could not ensure that we were delivering the pre-set FIO_2. Moreover, a recent study with the same system showed that, when delivering a FIO_2 of 100%, the effective delivered FIO_2 increases with flow rate and varies between 72.2% and 95% for flow rate from 0.4 L kg^{-1} $minute^{-1}$ to 2.5 L kg^{-1} $minute^{-1}$ (Jagodich *et al.* 2019). In our study, flow rate ranged from 0.44 to 1.84 L kg^{-1} $minute^{-1}$, so we can hypothesise that the effective FIO_2 did not reach 100%. Despite this limitation, our study confirms that HOT allows increase in PaO_2 in clinical settings.

In human medicine, several studies have showed a significant decrease of RR after initiation of HOT (Roca *et al.* 2010, Sztrymf *et al*. 2011, Sztrymf *et al*. 2012, Makdee *et al.* 2017). In our study, six dogs had a decrease in RR between T_0 and T_{60}, but with very variable evolution among time (Figure 5). The dogs were included in this study because of respiratory distress with failure to respond to nasal oxygen therapy, that could reasonably not resolve in one hour, especially as our population mainly had principally respiratory distress secondary to aspiration pneumonia. Finally, they were treated with HOT early in the course of their respiratory distress (30 min after admission), meaning that other treatments, such as diuretics, antibiotics, etc., did not have time to be effective. Mackdee *et al.* (2017) showed a significant decrease in RR after one hour in the HOT group compared to COT group in human patients with cardiogenic pulmonary oedema. Another study comparing RR between patients under nasal oxygen therapy or HOT in a more homogeneous population would be of great interest to differentiate between effects of time versus effects of treatment.

By enhancing the heating and humidification of nasal cavities, HOT has been shown to improve patient comfort in human medicine (Roca *et al.* 2010, Boyer *et al*. 2011, Sztrymf *et al.* 2012). In one veterinary study in hypoxemic dogs, HOT intolerance requiring sedation was noticed in 1/6 dogs (Keir *et al.* 2016). However, no TS was used in this study. Jagodich *et al.* (2019), using a different TS associated with a respiratory score, showed that HOT tolerance was inversely proportional to flow rate, and flow rate above 2.5 L minutes^{-1} were not well tolerated. In this study, the HOT administered with specific nasal cannula was easily tolerated and displayed very low TS during all the study period. It would have been interesting to compare tolerance of COT and HOT, but it was not the purpose of this study, and more studies on HOT tolerance are therefore needed. Moreover, one study in human medicine showed that temperature seems to significantly impact the comfort of dyspneic patients with high flows: for equal flow, patient

294 comfort was significantly higher at 31°C compared to 37°C (Mauri *et al.* 2018). The impact of
295 temperature was not evaluated in our pilot study and could be assessed in a larger population.

296 No clinically relevant complications related to the oxygen therapy technique were noted
297 during our study, which therefore supports previously published studies of HOT safety in dogs
298 (Keir *et al.* 2016, Daly *et al.* 2017, Jagodich *et al.* 2019). Jagodich *et al.* (2019) showed that at
299 flow rates above 2 L kg^{-1} $minute^{-1}$, dogs became less tolerant. Our study showed that lower flow
300 rate allowed improvement of oxygen parameters with good tolerance. However, in the study of
301 Daly *et al.* (2017), one dog had radiographic evidence of gastric distension, and in the study of
302 Jagodish *et al.* (2019), 8 out of 8 dogs had aerophagia noted on radiographs. As our dogs were
303 dyspneic, we did not perform any abdominal radiographs to evaluate the incidence of gastric
304 distension. Nevertheless, we did not notice any abdominal distension during physical examination.
305 Moreover, the potential long-term complications could not be assessed with our study design.

306 Given the inclusion criteria of severely dyspneic dogs, the mortality rate in our population
307 was high. In the study of Keir *et al.* (2016), 3 out of 6 dogs died, of those, 2 died as a result of
308 worsening hypoxemia. Our study population included various primary pulmonary disease
309 processes, that have a different prognosis (Hopper et al. 2007). However, both in Keir *et al.*
310 (2016) and in our study, aspiration pneumonia was the main diagnosis. Larger population is
311 needed to compare influence on mortality rate of HOT.

312 Some limitations should be noted in the current study. The biggest limitations are the small
313 sample size and the absence of control group that limits interpretation of the results. Our study
314 was designed as a pilot study for a future randomised controlled study. Adding the result of a
315 control group, treated with standard medical stabilisation and nasal oxygen therapy would have
316 been of great interest to provide context for the magnitude of improvement in recorded parameters
317 (i.e. effects of time versus treatment type). However, the dogs included in our study were severely
318 dyspneic, and not adding HOT to their therapeutic plan could have raised ethical concerns.

Second, HOT has been showed to have several physiological effects allowing improvement of PaO_2. In dogs, Jagodish *et al.* (2019) showed that HOT provides CPAP and predictable oxygen support in healthy dogs. As our study was a clinical study, it was not possible to use more invasive monitoring to differentiate between a positive effect on PaO_2 related to a therapeutic effect of the HOT on respiratory mechanic or related to enrichment of inspired oxygen. Third, the long-term implications of HOT were not evaluated, and our results (especially tolerance and complication) should be validated in a longer study. Finally, the inclusion of patients with different respiratory distress causes could have change the results, as some patients could benefit more or less from HOT.

Conclusion

This study is the first in veterinary medicine to prospectively confirm that HOT could deliver effective oxygenation and comfort with minimal complications in dyspneic dogs, and gives practical information on HOT use in dogs.

Bibliography

Boyer, A., Vargas, F., Delacre, M., *et al.* (2011) Prognostic Impact of High-Flow Nasal Cannula Oxygen Supply in an ICU Patient with Pulmonary Fibrosis Complicated by Acute Respiratory Failure. *Intensive Care Medicine* 37, 558-559

Briganti, A., Melanie, P., Portela, D., *et al.* (2010) Continuous positive airway pressure administered via face mask in tranquilized dogs. *Journal of Veterinary Emergency and Critical Care* 20, 503-508

Brown, J.E., Bersenas, A.M.E., Mathews, K.A., *et al.* (2009) Noninvasive ventilation in cats. *Journal of Veterinary Emergency and Critical Care* 19, 416-425

Daly, J.L., Guenther, C.L., Haggerty, J.M., *et al.* (2017) Evaluation of oxygen administration with a high-flow nasal cannula to clinically normal dogs. *American Journal of Veterinary Research* 78, 624-630

Di mussi, R., Spadaro, S., Stripoli, T., Volta, C.A., Trerotoli, P., Pierucci, P., Staffieri, F., Bruno, F., Camporota, L., Grasso, S. (2018) High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease. Critical Care 22, 180

Dunphy, E., Mann, F.A., Dodam, J., Branson, K., Wagner-Mann C., Johnson P., Brady M. (2002) Comparison of unilateral versus bilateral nasal catheters for oxygen administration in dogs. *Journal of Veterinary Emergency and Critical Care* 12, 245–251

Frat, J.P., Thille, A.W., Mercat, A., *et al.* (2015) High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *The New England Journal of Medicine* 372, 2185-2196

355 Guenther, C.L. (2019) Oxygen therapy In: Textbook of small animal emergency medicine. 1rst
356 edn. Eds K. Drobatz, K. Hopper; E. Rosanski and D. Silverstein. Wiley-Blackwell, Hoboken. pp
357 1177-1182

358 Grimm, K., Lamont, L., Tranquilli, W., *et al.* (2015) Anesthesia equipment. In: Veterinary
359 anesthesia and analgesia. 5th ed. Ames, Iowa, Wiley Blackwell. pp 23-85

360 Groves, N., Tobin, A. (2007) High flow nasal oxygen generates positive airway pressure in adult
361 volunteers. *Australian Critical Care: Official Journal of the Confederation of Australian Critical*
362 *Care Nurses* 20, 126-131

363 Hayes, G., Mathews, K., Doig, G., *et al.* (2010) The acute patient physiologic and laboratory
364 evaluation (APPLE) score: a severity of illness stratification system for hospitalized dogs. *Journal*
365 *of Veterinary Internal Medicine* 24, 1034-1047

366 Helviz, Y., Einav, S. (2018) A Systematic Review of the High-flow Nasal Cannula for Adult
367 Patients. *Critical Care* 22, 71

368 Hernández, G., Roca, O., Colinas, L. (2017). High-flow nasal cannula support therapy: new
369 insights and improving performance. *Critical Care* 21, 62

370 Hopper, K., Haskins, S.C., Kass, P.H., *et al.* (2007) Indications, management, and outcome of
371 long-term positive-pressure ventilation in dogs and cats: 148 cases (1990-2001). *Journal of the*
372 *American Veterinary Medical Association* 230, 64-75

373 Jagodich, T., Bersenas, A., Bateman, S., Kerr, C. (2019) Comparison of high flow nasal cannula
374 oxygen administration to traditional nasal cannula oxygen therapy in healthy dogs. Journal of
375 Veterinary Emergency and Critical Care DOI: 10.1111/vec.12817

376 Kallstrom, T.J. (2002) AARC Clinical Practice Guideline: oxygen therapy for adults in the acute
377 care facility--2002 revision & update. *Respiratory Care* 47, 717-720

Keir, I., Daly, J., Haggerty, J., *et al.* (2016) Retrospective evaluation of the effect of high flow oxygen therapy delivered by nasal cannula on PaO2 in dogs with moderate-to-severe hypoxemia. *Journal of Veterinary Emergency and Critical Care* 26, 598-602

Kilgour, E., Rankin, N., Ryan, S., *et al.* (2004) Mucociliary function deteriorates in the clinical range of inspired air temperature and humidity. *Intensive Care Medicine* 30, 1491-1494

Kopelman, A.E., Holbert, D. (2003) Use of Oxygen Cannulas in Extremely Low Birthweight Infants is Associated with Mucosal Trauma and Bleeding, and Possibly with Coagulase-negative Staphylococcal Sepsis. *Journal of Perinatology* 23, 94-97

Makdee, O., Monsomboon, A., Surabenjawong, U., *et al.* (2017) High-flow nasal cannula versus conventional oxygen therapy in emergency department patients with cardiogenic pulmonary edema: A Randomized Controlled Trial. *Annals of Emergency Medicine* 70, 465-472

Mazzaferro, E.M. (2015) Oxygen therapy. In: Small animal critical care medicine. 2dn edn. Eds K. Hopper and D. Silverstein. W.B. Saunders, Philadelphia. pp 77-80

Meira, C., Joerger, F.B., Kutter, A.P.N., Waldmann, A., Ringer, S.K., Böehm, S.H., Iff, S., Mosing, M. (2018) Comparison of three continuous positive airway pressure (CPAP) interfaces in healthy Beagle dogs during medetomidine-propofol constant rate infusions. *Veterinary Anaesthesia Analgesia* 45,145-157

Millar, J., Lutton, S., O'Connor, P. (2014) The use of high-flow nasal oxygen therapy in the management of hypercarbic respiratory failure. *Therapeutic Advances in Respiratory Disease* 8, 63-64

Mueller, E.R., (2007) Suggested Strategies for Ventilatory Management of Veterinary Patients with Acute Respiratory Distress Syndrome. *Journal of Veterinary Emergency and Critical Care* 11, 191-198

401 Parke, R.L., Eccleston, M.L., McGuinness, S.P. (2011) The effects of flow on airway pressure
402 during nasal high-flow oxygen therapy. *Respiratory Care* 56, 1151-1155

403 Staffieri, F., Crovace, A., De Monte,V. *et al.* (2014) Noninvasive continuous positive airway
404 pressure delivered using a pediatric helmet in dogs recovering from general anesthesia. *Journal of*
405 *Veterinary Emergency and Critical Care* 24, 578-585

406 Sumner, C., Rozanski, E. (2013). Management of respiratory emergencies in small animals. *The*
407 *Veterinary Clinics of North America Small Animal Practice* 43, 799-815

408 Sztrymf, B., Messika, J., Bertrand, F., *et al.* (2011) Beneficial effects of humidified high flow
409 nasal oxygen in critical care patients: a prospective pilot study. *Intensive Care Medicine* 37, 1780-
410 1796

411 Sztrymf, B., Messika, J., Mayot, T., *et al.* (2012). Impact of high-flow nasal cannula oxygen
412 therapy on intensive care unit patients with acute respiratory failure: A prospective observational
413 study. *Journal of Critical Care* 27, 324.e9-13

1	The patient is calm, comfortable; no agitation; no attempts to remove the nasal cannula
2	The patient tolerates the nasal cannula, but looks stressed and afraid; no attempts to remove the nasal cannula
3	The patient is agitated and tries to remove the nasal cannula; it is still possible to keep the nasal cannula on by gently restraining the patient
4	The patient does not tolerate the nasal cannula, is agitated, attempts to pull the nasal cannula; additional sedation is required to tolerate the oxygen delivery device

Table 1 : Oxygen delivery device tolerance score (adapted from Staffieri *et al.* 2014)

Figure 1: Schematic representation of a high-flow oxygen device and its components (Drawing Dr Mathieu Taroni).

Figure 2: Dog with the specific high-flow nasal cannula

Figure 3: Change in Arterial Partial Pressure of Oxygen (PaO_2) for individual patients. HOT: High-flow oxygen therapy. In figures 3, 4, 5 and supplemental material, the same dog is represented by the same colours.

Figure 4: Change in flow rates for individual patients. HOT: High-flow oxygen therapy.

Figure 5: Change in respiratory rates (RR) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Supplemental material

Figure 6: Change in pulse oxymetry (SpO_2) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Figure 7: Change in heart rates (HR) for individual patients. HOT: High-flow oxygen therapy. *Data from one dog are missing.*

Figure 8: Change in arterial partial pressure of CO_2 ($PaCO_2$) for individual patients. HOT: High-flow oxygen therapy.

Conflicts of interest statement

No conflicts of interest have been declared.