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STANDARD ARTICLE

The effect of inhaled heliox on peak flow rates in normal and brachycephalic dogs

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Background: Heliox, a mixture of helium and oxygen, alleviates airway obstruction in people and improves air flow, and its use has been proposed in dogs. Brachycephalic dogs have naturally occurring airway obstruction where heliox might be a useful therapeutic option.

Objective: The purposes of this study were to (1) determine the impact of breathing heliox on peak inspiratory and expiratory flows (PIF/PEF) in healthy dogs and (2) determine if brachycephalic dogs and mesocephalic dogs have similar responses to inhaled heliox.

Animals: Eleven healthy dogs: 5 mesocephalic and 6 brachycephalic dogs.

Methods: A prospective study. Tidal breathing flow-volume loops were recorded when dogs were breathing room air (nitrogen-oxygen) and heliox. Peak inspiratory and expiratory flow rates were recorded and the subjective shape of loops assessed. Peak inspiratory and expiratory flows pre- and post-heliox were compared using a Mann-Whitney Rank sum test with a *P*-value of <.05 considered significant.

Results: In inhaled heliox, PIF and PEF were evaluated by tidal breathing flow-volume loops. In mesocephalic dogs, PIF increased from a median of 820 mL/s (range, 494-1010 mL/s) to 1386 mL/s; *P* = .02; and for PEF from 688 mL/s to 1793 mL/s (*P* = .04), whereas in brachycephalic dogs, the median PIF increased from 282 mL/s to 694 mL/s; *P* = .01 and the median PEF increased from 212 mL/s to 517 mL/sec; *P* = .03. Brachycephalic dogs showed normalization of loop shapes.

Conclusions and clinical importance: Heliox improves flow rate and appears to improve flow patterns in brachycephalic dogs.

KEYWORDS

brachycephalic, heliox, pulmonary function testing, respiratory

1 | INTRODUCTION

Heliox is the name given to a gaseous mixture of helium and oxygen that has been used medically since the 1930s and is used to alleviate both upper and lower airway obstruction in people.[1–4] Flow through obstructed airways is turbulent, requiring increased effort to reach the desired tidal volume. Breathing heliox instead of room air reduces airway resistance because of the lowered density of helium. This property, therefore, favors the formation of laminar flow. By decreasing airway turbulence, heliox increases airflow, which subsequently decreases airway resistance and reduces work of breathing in patients with airway obstruction.[1,5]

Brachycephalic dogs have naturally occurring airway obstruction. Their features are described by the term brachycephalic airway obstructive syndrome (BAOS) and include stenotic nares, elongated soft palate, nasopharyngeal turbinates, everted laryngeal saccules, laryngeal collapse, and hypoplastic trachea.[4] These anatomic features cause characteristic changes in brachycephalic breathing patterns that can be identified with pulmonary function testing, including tidal breathing flow-volume loops (TBFVL).[6,7] Tidal breathing flow-volume loops are used to evaluate dogs and cats for airflow limitation.[6]

Abbreviations: BAOS, brachycephalic airway obstructive syndrome; PEF, Peak expiratory flow; PIF, Peak inspiratory flow; TBVFL, tidal breathing flow-volume loops.

Briefly, to perform TBFVL, a tight-fitting face mask is applied and connected to a pneumotachograph that measures flow. Flow is integrated to provide volume. The breathing pattern is objectively documented. Normally, peak inspiratory flow (PIF) is at the end of inspiration and peak expiratory flow (PEF) is at the beginning of expiration, with a normal loop appearing similar to a capital D. Inspiratory obstruction results in an early PIF and subsequent flow limitation, whereas expiratory obstruction results in limited PEFs. A fixed obstruction results in a truncated loop appearing more like a square.

Both partial and complete upper airway obstruction secondary to BAOS are not uncommon and would be expected to result in inspiratory obstruction. Heliox has been anecdotally suggested as a treatment for dogs with airway obstruction.[3] Heliox can be delivered in a cage, or via a face mask, and has appeal as a therapeutic agent due to ease of administration and rheological characteristics. However, no clinical trials have evaluated the utility of heliox in pet dogs with or without airway obstruction.

The goal of this study was to assess the effect of heliox (70% helium/30% oxygen) versus nitrox (79% nitrogen/21% oxygen) on TBFVL in mesocephalic and brachycephalic dogs. Our hypothesis was that higher peak flow rates would be achieved after spontaneous ventilation with heliox as compared to nitrox, and that these effects would be more pronounced in brachycephalic dogs with naturally occurring airway obstruction.

2 | MATERIALS AND METHODS

2.1 | Dogs

Healthy mesocephalic and brachycephalic dogs were recruited from the hospital community for this prospective study. Eligible dogs were required to have a normal physical examination for their breed and no history of respiratory disease before study inclusion. No sedated oral examination was performed to establish airway normalcy. Brachycephalic dogs showed naturally occurring upper airway obstruction secondary to their conformation although they were considered clinically normal by their owners. Brachycephalic dogs that had undergone palliative surgery (eg, palatoplasty) were excluded from enrollment. Age, sex, breed, and body weight were recorded for each dog. The study was approved by the Clinical Science Review Committee and the owners provided written, informed consent.

2.2 | Tidal breathing flow-volume loops

For measurement of TBFVL, dogs wore a tight-fitting face mask connected to a pneumotachograph and an associated pressure transducer. The same face mask was used for all dogs. The pressure signal was then amplified and plotted on an X-Y recorder. Electrical integration of the flow signal was used to obtain inhaled and exhaled gas volumes, which were then plotted against flow. The apparatus was calibrated with room air using a 500 mL syringe. The data were recorded using a software program (Buxco Electronics; Data Sciences International [DSI], St. Paul, Minnesota) and subsequently imported to a statistical program for analysis (Released 2015, IBM SPSS Statistics for Windows, Version 24.0; IBM Corp, Armonk, New York). Flow data for heliox was converted based upon a conversion factor to account for viscosity differences using standard conversion techniques.[1,2] A conversion factor was chosen to account for differences in flow rate as measured by the apparatus given the different characteristics of the gases. Unfortunately, this was performed post hoc, and it would have been ideal to perform calibration using the various gas mixtures real time. Conversions are required to account for the differences in viscosity of the gases. Flowmeters (eg, Pneumotachographs) measure the flow by determining the pressure drop during laminar flow. Gases with altered viscosity (eg, Helium) have higher actual flow rates than what pneumotachograph calibrated to room air would determine.

Testing was performed on each dog in either a standing or sitting position without sedation. Each dog received both heliox (70% helium/30% oxygen) and nitrox (79% nitrogen/21% oxygen) in a randomized order for at least 2 minutes via a nonbreathing valve and 10-L bag, with a minimum washout period of 15 minutes between tests.

For data analysis, the mean measurements for 5-10 consecutive breaths were reported. Portions with respiratory rates greater than 60 breaths/min were excluded due to difficulty in evaluating TBFVL while panting. Loops with inspiratory and expiratory volumes differing >5% were excluded from the analysis. The loops were evaluated for qualitative shape, inspiratory time (T_i), expiratory time (T_e), PIF, and PEF.

The effect of heliox versus nitrox on respiratory variables within each group (brachycephalic or mesocephalic) was compared using Mann-Whitney Rank Sum test with $P < .05$ considered statistically significant.

3 | RESULTS

Eleven healthy adult dogs were enrolled. Five mesocephalic breeds (2 German Shepherd dogs, 1 Belgian Malinois, 1 Golden Retriever, and 1 Pointer-Labrador cross) and 6 brachycephalic breeds (3 Boston Terriers, 2 Pugs, and 1 English Bulldog) were evaluated. The mean body weights were 44.7 ± 8.7 kg in the mesocephalic group and 11.9 ± 3.9 kg in the brachycephalic group.

Each dog tolerated testing well, and no dogs were excluded from data calculation. Median (range) for T_i, T_e, PIF, and PEF were determined for both mesocephalic and brachycephalic dogs (Table 1). Within the mesocephalic group, there was no significant change in T_i (P = .83) or T_e (P = .83) between heliox and nitrox. There were, however, significant increases in PIF (P = .02) and PEF (P = .04) when this group was administered heliox. Similarly, within the brachycephalic group, there was no significant change in T_i (P = .30) or T_e (P = .38) between heliox and nitrox. Brachycephalic dogs also showed a significant increase in PIF (P = .01) and PEF (P = .03) when breathing heliox. The percentage change in inspiratory and expiratory flow rates was not different between groups although the subjective loop shape appeared different between brachycephalic and mesocephalic dogs. (Figure 1).

TABLE 1 Ventilatory parameters (median and range) in awake dogs associated with breathing nitrox or heliox, compared by Mann-Whitney U tests

Parameters	RR (breaths/min)	T_i (s)	T_e (s)	PIF (mL/s)	PEF (mL/s)
Mesocephalic					
Nitrox	23 (20-43)	1.01 (0.88-1.52)	1.54 (1-2.8)	820 (494-1010)	688 (467-1026)
Heliox	24 (11-62)	0.97 (0.46-1.61)	1.46 (0.50-3.8)	1386 (459-1695)	1793 (1001-1880)
P	.83	.83	.83	.02*	.04*
Brachycephalic					
Nitrox	23 (16-37)	1.44 (0.73-1.60)	1.42 (0.86-2.06	282 (148-341)	212 (90-536)
Heliox	30 (19-35)	0.91 (0.65-1.76	1.16 (0.94-1.39)	694 (375-988)	517 (357-1058)
P	.58	.30	.38	.01*	.03*

Abbreviations: PIF, peak inspiratory flow; PEF, peak expiratory flow; RR, respiratory rate; T_i, inspiratory time; T_e, expiratory time.
*<0.05.

4 | DISCUSSION

This study demonstrates significant increases in airway flow rate during tidal breathing of heliox in healthy mesocephalic and brachycephalic dogs. These changes can be attributed to the low density of heliox causing an increase in laminar flow and a subsequent decrease in airway resistance. Qualitatively, the contour of the room air brachycephalic TBFVL had flattened inspiratory and expiratory loops, which normalized when breathing heliox, although the changes in PIF and PEF were not significantly different between brachycephalic and mesocephalic dogs. Unfortunately, more objective criteria of loop appearance were not available. Based on this finding, heliox appeared to partially overcome naturally occurring upper airway obstruction in brachycephalic dogs and increased flow rates throughout the respiratory tract in both mesocephalic and brachycephalic dogs.

Despite the lack of a difference between confirmation groups, there was a significant increase in PIF and PEF within both study groups when breathing heliox, supporting the conclusion that airway resistance decreases with heliox use. The mesocephalic dogs were significantly larger than the brachycephalic dogs, but simple percentage increases in flow rates were seen between both groups.

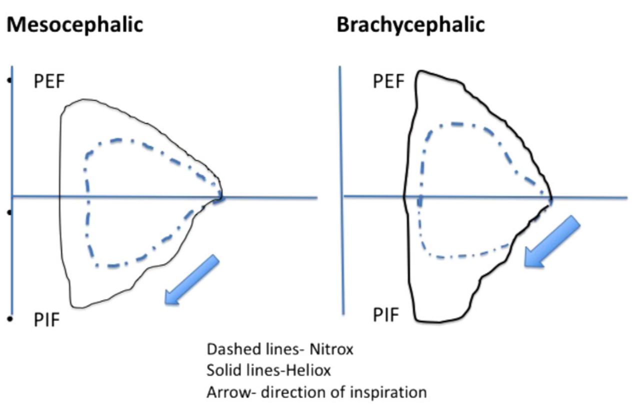

FIGURE 1 Representative tidal breathing flow-volume loops from mesocephalic and brachycephalic dogs while breathing nitrox or heliox. The solid line indicates heliox and the dashed line nitrox. The loop for the mesocephalic dog has a PIF and PEF of the heliox loop of 1250 mL/s, whereas the brachycephalic dog has 500 mL/s; the flow rate is also influenced by size. PIF, peak inspiratory flow; PEF, peak expiratory flow

Factors affecting the results of TBFVL include system leaks (particularly at the mask), panting, and respiratory effort. For this study, a tight-fitting wide face mask with little to no dead space was used for pulmonary function testing in brachycephalic dogs. The loops used had <5% difference between the inspiratory and expiratory volumes, demonstrating a sealed system without leakage. Respiratory effort can change the contour of TBFVL. The loops recorded for this study were visually similar in contour and shape to previously described loops for both brachycephalic and normal dogs.[6–8] Unfortunately, more objective criteria of loop shape difference were not recorded.

There are several limitations to this study. No airway examinations were performed in any dog. Therefore, the extent of airway obstruction could not be visually assessed in the brachycephalic group. There were, however, characteristic changes in TBFVL in the brachycephalic dogs that were consistent with upper airway obstruction. Elevated airway resistance is the cause of chronic intermittent respiratory distress in brachycephalic dogs. In this study, we used flow as a surrogate for resistance. Considering that heliox decreases the work of breathing through obstructed airways,[1,5] airway pressure was likely also decreased, further reducing airway resistance.

Additionally, the system was calibrated based upon room air and corrected for known changes based on the characteristics of heliox. It would have been ideal to calibrate the flowmeter specifically for heliox, but due to technical constraints, the decision was made to use a correction factor. Post hoc calibration showed consistent results with what the correction factor suggested, but ideally, and in future studies, equipment calibration should be performed at the point of the study. Finally, a relatively small number of dogs were enrolled, and brachycephalic dogs were considered minimally affected. No oral examination was performed under sedation; this would have helped to clarify the abnormalities present. A larger sample size or enrollment of more severely affected dogs might have identified statistically significant flow changes between mesocephalic and brachycephalic dogs.

One potential adverse effect of heliox treatment in dogs is hypothermia due to increased flow rate.[9] Temperature was not recorded in the dogs in this study due to the short duration of heliox inhalation; however, in clinical cases, monitoring temperature might be important. This effect could be advantageous, as many dogs with upper airway obstruction are hyperthermic due to relative inability to cool.[8,10]

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

The study was approved by the Clinical Science Review Committee, and the owners provided informed consent.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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