Effects of tidal volume, ventilatory frequency, and oxygen insufflation flow on the fraction of inspired oxygen in cadaveric horse heads attached to a lung model

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Objective—To measure the effects of tidal volume, ventilatory frequency, and oxygen insufflation flow on the fraction of inspired oxygen in cadaveric horse heads attached to a lung model.

Sample—8 heads of equine cadavers.

Procedures—Each cadaveric horse head was intubated with a nasotracheal tube that extended into the proximal portion of the trachea. Oxygen was delivered through an oxygen catheter contained within and extending to the tip of the nasotracheal tube. The trachea was connected to the lung model by use of a spiral-wound hose with a sampling adaptor. Eight treatment combinations involving 2 tidal volumes (5 and 8 L), 2 ventilatory frequencies (6 and 12 mechanical breathes/min), and 2 insufflation rates (10 and 15 L/min) were applied to each head. Hand-drawn inspired gas samples were collected and analyzed for oxygen concentrations.

Results—The fraction of inspired oxygen (measured at mid trachea) ranged from 26.8% to 39.4%. Fraction of inspired oxygen was significantly higher with a smaller tidal volume, lower ventilatory frequency, and higher insufflation rate.

Conclusions and Clinical Relevance—In the study model, measured fraction of inspired oxygen varied with ventilatory pattern as well as oxygen insufflation rate. Clinically, this information could be beneficial for interpretation of data regarding arterial blood gases and hemoglobin saturation and in making appropriate oxygen insufflation decisions for anesthetized horses that are breathing room air. (Am J Vet Res 2012;73:134–139)
esthesis, compared with findings in those horses when no supplemental oxygen insufflation was provided. Development of hypoxemia was avoided in horses with supplemental oxygen insufflation.\textsuperscript{12} Results of multiple studies\textsuperscript{9–11} have indicated that the use of an oxygen insufflation flow helps prevent hypoxemia in horses during recovery from anesthesia. Although a higher oxygen insufflation flow helps prevent hypoxemia in horses during recovery from anesthesia, studies have not been conducted to measure the Fi\textsubscript{O\textsubscript{2}} during nasal insufflation in recumbent anesthetized horses, to our knowledge. This measurement would provide valuable information for clinicians applying insufflation techniques. Additionally, the effects of different respiratory patterns on Fi\textsubscript{O\textsubscript{2}} have not been determined. Wilson et al\textsuperscript{12} measured the Fi\textsubscript{O\textsubscript{2}} in healthy and respiratory tract–compromised standing horses (ie, horses with recurrent airway obstruction). Several flow rates of supplemental oxygen were used, and in all horses, an increase in oxygen insufflation flow was directly related to increases in measured Fi\textsubscript{O\textsubscript{2}} and Pa\textsubscript{O\textsubscript{2}}. Respiratory tract–compromised horses have higher ventilation perfusion inequality, increased respiratory rate, and increased peak inspiratory flow. Compared with healthy horses, this contributes to differences in measured Fi\textsubscript{O\textsubscript{2}} and Pa\textsubscript{O\textsubscript{2}}.\textsuperscript{12} Evidently, an increase in supplemental oxygen flow rate increases Pa\textsubscript{O\textsubscript{2}} and decreases the likelihood of hypoxemia. Variables other than insufflation flow may alter the fractional concentration of inspired oxygen, which may affect the Pa\textsubscript{O\textsubscript{2}}. Accumulation of insufflated oxygen in the anatomic dead space of a horse's head is dependent on time during the expiratory pause. Increases in time would allow more insufflated oxygen to displace the expired gas in the anatomic dead space in the head. Inspired oxygen concentration can also be altered by inspiratory time as well as total inspiratory volume. Changes in these variables may affect the Fi\textsubscript{O\textsubscript{2}}.

The purpose of the study reported here was to measure the Fi\textsubscript{O\textsubscript{2}} of an animal on the basis of the oxygen flow chosen and the characteristic of the respiratory pattern allows a clinician to better interpret arterial blood gas data from anesthetized as well as respiratory tract–compromised standing horses and to adjust treatments and conditions accordingly.

**Materials and Methods**

**Model**—The study involved use of 8 cadaveric horse heads attached to a lung model (Figure 1). In each of the 8 cadavers, the head was severed from the neck at the fourth cervical vertebra. Heads were harvested from mature Quarter Horses (age range, 10 to 31 years; mean ± SD age, 14.6 ± 6.8 years) that weighed 371 to 575 kg (mean weight, 487 ± 70 kg) and were euthanized due to medical conditions via IV injection of pentobarbital. Heads were measured from the occipital crest to the rostralmost aspect of the muzzle (57 to 64 cm; mean, 60.5 ± 2.7 cm). Heads were placed right-side down with the nares and mouth unobstructed. An oxygen insufflation catheter, constructed from a 2.1-m-long piece of oxygen tubing,\textsuperscript{6} was inserted through the lumen of a cuffless nasotracheal tube (internal diameter, 20 mm) and permanently attached to the distal tip of the tube with multifilament nylon suture. The cuffless nasotracheal tube with oxygen insufflation catheter was passed through the left naris and positioned in the proximal portion of the trachea. The insufflation catheter was attached to a 15-L oxygen flowmeter.\textsuperscript{6} The flowmeter was calibrated prior to the beginning of the study by use of a recently serviced and calibrated ventilometer.\textsuperscript{6}

The lung model consisted of a corrugated rubber bellows driven by a pneumatic piston. The outlet from the bellows assembly consisted of a chlorinated polyvinyl chloride tube (external diameter, 1.25 inches). The lung model was connected to the cadaver head by a spiral-wound tube (internal diameter, 1.25 inches). The proximal end of the spiral-wound tubing was attached to a junction adaptor with a sampling port. The junction adaptor was secured to the trachea with a stainless steel compression clamp, forming a gastight seal. The pneumatic piston was cycled with a controller that determined ventilatory frequency and rhythm. The piston was equipped with preset stops to deliver the selected tidal volume. The bellows was set to deliver a tidal volume of either 5 or 8 L in a to-and-fro manner through the cadaver head, thereby simulating a normal breathing pattern. Inspiratory time, depending on the tidal volume, varied between 1 and 1.5 seconds. A port connector was mounted in the top of the bellows’ driving plate for insufflation of carbon dioxide from a precision carbon dioxide flowmeter.\textsuperscript{4} Carbon dioxide was insufflated into the bellows at a rate of 1 L/min to account for estimated minute carbon dioxide production in a 450-kg horse.\textsuperscript{13} Because carbon dioxide was added at the rate of 1 L/min to the circuit, oxygen delivery through the insufflation catheter was reduced by 1 L/
min to account for expected oxygen consumption. The resulting total insufflated volume of oxygen and carbon dioxide into the model was 10 or 15 L/min.

Sample collection and analysis—Settings on the lung model were adjusted for the selected treatment, and a 10-minute equilibration time was allowed prior to sample collection. Hand-drawn samples were collected from the sampling port by use of a 60-mL syringe. Samples were aspirated during the entire inspiratory phase of ventilation in 20-mL aliquots during 3 ventilatory cycles (total volume, 60 mL). Three 60-mL samples were acquired for each treatment. The FiO₂ was determined with an electrochemical oxygen analyzer. The oxygen analyzer was calibrated according to the manufacturer’s instructions prior to each experiment. End-tidal gas samples were collected for carbon dioxide analysis during the expiratory pause in the same manner as described and analyzed with a gas monitor.

Treatments and variable selection—Each cadaveric horse head received each of 8 treatments in random order. Treatments consisted of a combination of 3 conditions: tidal volume (5 or 8 L), ventilatory frequency (6 or 12 mechanical breaths/min), and insufflation flow (10 or 15 L/min). Tidal volumes were selected on the basis of multiple tidal volume measurements from each of 5 horses anesthetized for routine clinical procedures and in which anesthesia was maintained with a constant rate infusion of guaifenesin, ketamine hydrochloride, and xylazine hydrochloride at Kansas State University Veterinary Medical Teaching Hospital prior to beginning the study. The mean tidal volume was calculated, and on the basis of the associated 95% confidence interval, the 2 treatment tidal volumes were chosen. Tidal volume was measured after horses were intubated endotracheally with a tube (internal diameter, 26 mm) and allowed to spontaneously ventilate. Expired gas was collected by attaching a 3-way valve to the endotracheal tube and collecting expiratory gases in a polyethylene bag. Expired gas was collected for approximately 1 minute. The number of complete breaths was counted, and the total volume collected was divided by the number of breaths collected to determine a mean tidal volume. The total gas collected was measured with a precision gas meter. Tidal volumes of 5 and 8 L were determined to be clinically representative of the volumes measured.

Ventilatory frequencies used in the study were 6 or 12 mechanical breaths/min. Ventilatory frequencies were selected on the basis of 36 randomly chosen records of horses in which anesthesia was maintained with a constant rate infusion of guaifenesin, ketamine, and xylazine at Kansas State University Veterinary Medical Teaching Hospital in 2007 through 2009. The mean respiratory frequency was calculated, and on the basis of the associated 95% confidence interval, the 2 treatment ventilatory frequencies were chosen. Ventilatory frequencies of 6 and 12 mechanical breaths/min were determined to be clinically representative of respiratory frequencies in anesthetized horses. Oxygen insufflation flows were selected on the basis of data obtained in previous studies.

Statistical analysis—The study was organized in a randomized complete block design with the blocking factor being the 8 cadaveric horse heads with subsampling within each treatment-block combination. The treatment structure was a 3-factor factorial with factors of tidal volume (5 or 8 L), ventilatory frequency (6 or 12 mechanical breaths/min), and insufflation rate (10 or 15 L/min). After verification of normality by use of a univariate procedure, data were analyzed by use of an ANOVA with a mixed general linear models procedure, and values of P < 0.005 were considered significant. The tidal volume, ventilatory rate, and oxygen flow main effects and resulting interactions were tested by use of the following calculation: tidal volume × ventilatory frequency × insufflation rate × horse head. Data are expressed as least squares mean ± SE for each level of the 3 factors.

Results

Fractions of inspired oxygen during the 8 treatment combinations applied to each cadaveric horse head were determined (Table 1). The FiO₂ of the 2 selected treatments (6 vs 12 mechanical breaths/min, 5 vs 8 L, and 10 vs 15 L/min) within the same variable (ventilatory frequency, tidal volume, and insufflation rate) were assessed (Table 2). A comparison between each selected variable as an independent factor indicated that the FiO₂ was higher with a lower ventilatory frequency, smaller tidal volume, and higher oxygen insufflation rate. The FiO₂ was significantly (P < 0.001)
different between each simple effect. No interaction was detected among the factors. The lack of interaction between the factors indicated that a lower respiratory rate will result in a higher FiO₂, than that achieved with a higher respiratory rate, independent of the tidal volume or oxygen insufflation rate. Furthermore, a smaller tidal volume will result in a higher FiO₂ than that achieved with a larger tidal volume, independent of a horse’s respiratory rate or oxygen insufflation rate. Similarly, a higher oxygen insufflation rate will always result in a higher FiO₂ than that achieved with a lower oxygen insufflation rate, independent of the respiratory variables. 

**Discussion**

Results of several studies have indicated that anesthetized horses breathing room air will become hypoxic. The use of supplemental oxygen insufflation decreases the risk of hypoxemia by increasing the FiO₂, making it’s use the standard of care in horses anesthetized by use of parenterally administered drugs and during recovery from anesthesia. Although higher oxygen insufflation rates are known to result in higher PaO₂ values, no studies have been performed to analyze whether respiratory patterns also affect PaO₂. The results of the present study involving cadaveric horse heads attached to a lung model indicated that the concentration of inspired oxygen during oxygen insufflation depends on the insufflated oxygen flow selected as well as respiratory rate and tidal volume. Accurate measurement of inspired gases can be challenging. Few studies have included measurement of the FiO₂, in horses during supplemental oxygen insufflation, and those studies were performed on standing horses instead of anesthetized recumbent horses. There are 2 reasons why measurement of FiO₂ is challenging. First, accurate determination of the FiO₂ requires continuous gas collection from the mid portion of the trachea. In a living horse, this is an invasive procedure, possibly resulting in site infection or tracheal damage. Second, during oxygen insufflation, gas samples must be collected continuously during the entire inspiratory phase because the FiO₂ is constantly changing. The gas collected during the beginning of inspiration has a higher concentration of oxygen than the gas collected at the end of inspiration. We believe that the model we used in the present study reflects the way air moves and accumulates in nasal and oral cavities and Airways during ventilation. The use of a 20-mm internal diameter cuffless nasotracheal tube allows gas (air and oxygen) to pass through as well as around the nasotracheal tube during inspiration and expiration, thereby enhancing oxygen accumulation. The advantages of the use of a nasotracheal tube during insufflation are that a patent airway is maintained during anesthesia as well as during the recovery period, and the insufflation catheter can be passed more distally into the airway, thereby avoiding nasopharyngeal delivery of oxygen. The use of a nasotracheal tube is a standard practice in our facility and is recommended for our field service units.

Oxygen insufflation provides continuous flow during the entire respiratory cycle. During the expiratory pause, oxygen accumulates in the nasal and oral cavities. With a low respiratory rate, the expiratory pause is longer, providing more time for the insufflated oxygen to displace the expired gas that accumulated in the nasal and oral cavities and thereby raising the oxygen concentration. In the present study, a higher FiO₂ was associated with the lower ventilatory rate. A ventilatory rate of 6 mechanical breaths/min generated an FiO₂ that was 19.9% higher than that generated by a ventilatory rate of 12 mechanical breaths/min. Smaller tidal volumes should also result in a higher FiO₂ because less room air is inspired; therefore, the oxygen that accumulated in the nasal and oral cavities during the expiratory pause will be a higher proportion of the following inspired tidal volume. This was confirmed in the present study; a 5-L tidal volume resulted in an FiO₂ that was 13.1% higher than that generated when an 8-L tidal volume was used. A higher insufflation rate with no change in minute ventilation should result in a higher FiO₂ because a higher flow will displace more gas from the nasal and oral cavities during the expiratory pause. This was also confirmed on the basis of the study data; when tidal volume and ventilatory rate remained constant, a higher oxygen insufflation rate (15 L/min) resulted in an FiO₂ that was 9.5% higher than that generated when the lower rate oxygen insufflation was used (10 L/min).

In the present study, data were analyzed as independent factors; therefore, minute ventilation (tidal volume X ventilatory rate) was not analyzed. On the basis of the study results, it is likely that, under most circumstances, lower minute ventilation would result in a higher FiO₂. However, such a conclusion cannot be made on the basis of the design and data analysis of this study. Low minute ventilation also results in an increase in PaCO₂, which, based on the alveolar gas equation, would lead to a decrease in partial pressure of alveolar oxygen and ultimately a decrease in PaO₂. High PaCO₂ could then potentially be a cause for reduced PaO₂ and limit the expected effects of supplemental oxygen insufflation. With the use of this equine model, it was not possible to assess the effect of minute ventilation on PaO₂.

The present study was conducted because we were interested in examining the effect of tidal volume and respiratory rate on FiO₂ in horses; however, the use of a lung model was necessary because live horses do not permit control of tidal volume or respiratory rate. To determine and control the desired conditions, we used cadaver horse heads and an artificial lung model. Unfortunately, with the use of a model, measurement of PaO₂ was not possible. Collection of arterial blood samples and measurement of PaO₂ would be the only in vivo method to determine whether higher FiO₂ results in a similar increase in PaO₂ and avoidance of hypoxemia. On the basis of the study findings, we cannot conclude that smaller tidal volumes or lower respiratory rates would necessarily result in higher PaO₂ in parenterally anesthetized horses and horses subsequently recovering from anesthesia. However, with consideration of the study results, clinicians may be able to more accurately estimate FiO₂ when analyzing arterial blood gas data and interpreting PaO₂ measurements in anesthetized or recovering horses that are receiving oxygen supplementation. Observation of the respiratory
pattern might also alert veterinarians that they should increase oxygen insufflation flow with rapid breathing or large breaths.

In the present study, carbon dioxide was insufflated into the bellows at a rate of 1 L/min to account for carbon dioxide production in an anesthetized horse. Adding 1 L of carbon dioxide to the lung model increased the total insufflated volume; thus, we reduced the insufflated oxygen rate to either 9 or 14 L/min to simulate oxygen consumption of 1 L/min. The result was an insufflation rate of 15 L/min (1 L of carbon dioxide/min plus 14 L of oxygen/min) or 10 L/min (1 L of carbon dioxide/min plus 9 L of oxygen/min).

Subtraction of 1 L/min from the oxygen insufflation rate allowed us to maintain the total insufflation rates at 15 and 10 L/min rather than at 16 and 11 L/min. Nevertheless, either combination of rates could have been used, both with advantages and disadvantages. By maintaining the total insufflation rate at 10 or 15 L/min (commonly used flow rates), we allowed the accumulation in the nasal and oral cavities to occur at a rate consistent with current clinical usage and less likely to alter the oxygen-to-room air ratio that would accumulate in the nasal and oral cavities. The disadvantage was that ultimately a lower amount of oxygen was insufflated (14 L/min instead of 15 L/min and 9 L/min instead of 10 L/min). By use of a total insufflation rate of 11 or 16 L/min (14 or 15 L/min of oxygen with 1 L/min of carbon dioxide), the oxygen flow would be as described in previous studies, but the disadvantage would be that a higher total insufflation rate would displace more gas from the oral and nasal cavities during the expiratory pause. This would erroneously increase the inspired oxygen concentration during the beginning of inspiration. In the present study, carbon dioxide was insufflated into the bellows, and the end-tidal CO₂ concentration was measured during each treatment. The sole purpose of measuring the end-tidal CO₂ concentration was to use it as a marker of minute ventilation because it should increase or decrease depending on the administered treatment.

Animal size may also be a factor in the FIO₂ generated. In the present study, heads were harvested from adult Quarter Horses of similar body sizes. The size of the head, and therefore size of the nasal and oral cavities, dictates the space available for oxygen to accumulate during the expiratory pause. Larger heads with larger nasal and oral cavities should, in theory, allow for greater oxygen accumulation and therefore higher FIO₂. Unfortunately, even though head lengths were measured, we did not measure the combined volume of the nasal and oral cavities. Thus, we cannot determine whether it would be a significant factor in the measured FIO₂ values. In retrospect, measurement of the volume of the nasal and oral cavities with a water displacement method would have been desirable. Other limitations of the study were associated with the need to use a model instead of living horses. Limitations such as the inability to measure PaO₂ and PaCO₂ and the inability to simulate additional clinical breathing patterns leave important questions unanswered.

Horses benefit from administration of supplemental oxygen during anesthesia. Horses hospitalized because of respiratory tract compromise are similarly benefited by such treatment. In equine patients, characterization of respiratory pattern and awareness of the insufflation rate of supplemental oxygen provided may allow clinicians to more accurately estimate FIO₂. This estimation should result in a more accurate calculation of the alveolar-arterial PO₂ gradient and may help in making case management decisions. Clinicians could better understand changes in PaO₂ measurement even during constant oxygen flow delivery.

Undoubtedly, to avoid hypoxemia, supplemental oxygen should be provided to horses during parenteral anesthesia as well as during recovery from anesthesia. It should be noted that the FIO₂ is dependent not only on the insufflation flow selected but also on respiratory rate and tidal volume. Results of other studies have indicated that there is large variability in PaO₂ in horses during recovery from anesthesia even with the same oxygen insufflation flow. This could be, in part, explained by different respiratory rates and tidal volumes or a lack of consistency in the location of the insufflation catheter tip within or between studies. A horse’s respiratory rate and tidal volume cannot be controlled by anesthetists; therefore, oxygen insufflation flow rates of ≥ 15 L/min are still recommended. The new information provided in present study will allow clinicians to be more knowledgeable and better prepared when using nasal oxygen insufflation, selecting the oxygen flow, and, if applicable, interpreting blood gas analysis results for horses.

References

b. Western Medica, Westlake, Ohio.
c. Ohmeda Ventilometer, RM 211, Datex-Ohmeda Inc, Madison, Wis.
e. Teledyne AX 350 oxygen analyzer, Teledyne, City of Industry, Calif.
f. Datex-Ohmeda CardioCap5 gas monitor, General Electric Co, Datex-Ohmeda, Madison, Wis.
h. DTM-325 gas meter, American Meter Co, Horsham, Pa.
i. PROC MIXED, SAS, version 9.1, SAS Institute Inc, Cary, NC.


