Effects of inspired oxygen concentration on ventilation, ventilatory rhythm, and gas exchange in isoflurane-anesthetized horses

Mariana N. Crumley, DVM; Rose M. McMurphy, DVM; David S. Hodgson, DVM; Scott E. Kreider, MS

Objective—To compare the effects of 2 fractions of inspired oxygen, 50% and >95%, on ventilation, ventilatory rhythm, and gas exchange in isoflurane-anesthetized horses.

Animals—8 healthy adult horses.

Procedures—In a crossover study design, horses were assigned to undergo each of 2 anesthetic sessions in random order, with 1 week separating the sessions. In each session, horses were sedated with xylazine hydrochloride (1.0 mg/kg, IV) and anesthesia was induced via IV administration of diazepam (0.05 mg/kg) and ketamine (2.2 mg/kg). Anesthesia was subsequently maintained with isoflurane in 50% or >95% oxygen for 90 minutes. Measurements obtained during anesthesia included inspiratory and expiratory peak flow and duration, tidal volume, respiratory frequency, end-tidal CO2 concentration, mixed expired partial pressures of CO2 and O2, PaO2, PaCO2, blood pH, arterial O2 saturation, heart rate, and arterial blood pressure. Calculated values included the alveolar partial pressure of oxygen, alveolar-to-arterial oxygen tension gradient ($P_{A}O_{2} - PaO_{2}$), rate of change of $P_{A}O_{2} - PaO_{2}$, and physiologic dead space ratio. Ventilatory rhythm, based on respiratory rate and duration of apnea, was continuously observed and recorded.

Results—Use of the lower inspired oxygen fraction of 50% resulted in a lower arterial oxygen saturation and PaO2 than did use of the higher fraction. No significant difference in PaCO2, rate of change of $P_{A}O_{2} - PaO_{2}$, ventilatory rhythm, or other measured variables was observed between the 2 sessions.

Conclusion and Clinical Relevance—Use of 50% inspired oxygen did not improve the ventilatory rhythm or gas exchange and increased the risk of hypoxemia in spontaneously breathing horses during isoflurane anesthesia. Use of both inspired oxygen fractions requires adequate monitoring and the capacity for mechanical ventilation. (Am J Vet Res 2013;74:183–190)

Several anesthetic-related complications occur with greater frequency or magnitude in horses than in other species. Among these complications are hypoventilation1-2 and a large $P_{A}O_{2} - PaO_{2}$, which may result in hypoxemia despite high inspired oxygen concentrations.3-5

Hypoventilation, described as an increase in PaCO2 to >45 mm Hg, is a problem that can develop during equine inhalation anesthesia and, to a lesser degree, during total IV anesthesia.1-2 The increase in PaCO2 during isoflurane anesthesia is attributable to a decrease in respiratory rate, whereas tidal volume is maintained or increases.1-6 Horses anesthetized with isoflurane in 100% oxygen often have an irregular ventilatory rhythm, characterized by a low respiratory rate with prolonged periods of apnea.1-6,7 Anesthetized

### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>ETISO</td>
<td>End-tidal isoflurane concentration</td>
</tr>
<tr>
<td>$P_{E}O_{2}$</td>
<td>Fractional expired oxygen concentration</td>
</tr>
<tr>
<td>$P_{I}O_{2}$</td>
<td>Fractional inspired oxygen concentration</td>
</tr>
<tr>
<td>$P_{A}O_{2} - PaO_{2}$</td>
<td>Alveolar-to-arterial oxygen tension gradient</td>
</tr>
<tr>
<td>$P_{A}O_{2}$</td>
<td>Alveolar partial pressure of oxygen</td>
</tr>
<tr>
<td>$P_{E}CO_{2}$</td>
<td>Mixed expired partial pressure of carbon dioxide</td>
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<tr>
<td>PEEP</td>
<td>Positive end-expiratory pressure</td>
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<tr>
<td>$P_{E}O_{2}$</td>
<td>Mixed expired partial pressure of oxygen</td>
</tr>
<tr>
<td>$P_{I}O_{2}$</td>
<td>Inspired partial pressure of oxygen</td>
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<tr>
<td>$SaO_{2}$</td>
<td>Arterial oxygen saturation</td>
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<tr>
<td>$V_{D}/V_{T}$</td>
<td>Physiologic dead space ratio</td>
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</table>

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horses with the irregular ventilatory rhythm combined with the increase in PaCO₂ often benefit from intermittent positive pressure ventilation; however, this intervention may cause a decrease in cardiac output. Horses anesthetized with halothane in 30% oxygen have a lower PaCO₂ than do horses anesthetized with halothane in 85% oxygen, and horses anesthetized with tiletamine-zolazepam hypoventilate to a greater degree when anesthesia is maintained at an inspired oxygen concentration of > 95% versus 21%. A large PaO₂ - PaO₂ is a common clinical finding in anesthetized horses and has been reported for spontaneously breathing and mechanically ventilated horses. Horses can become hypoxemic (PaO₂ < 60 mm Hg) even while breathing 100% oxygen. The large PaO₂ - PaO₂ is usually the result of ventilation perfusion mismatch and intrapulmonary shunting caused by atelectasis formation. Pulmonary shunting in anesthetized horses reportedly increases by 21% to 31% (mean, 34%), compared with 4% to 7% in standing horses prior to anesthesia. Furthermore, administration of a high concentration of inspired oxygen (> 95%) during anesthesia in horses has been associated with an increase in intrapulmonary shunting and a decrease in gas exchange.

Airway closure and atelectasis formation in humans can be responsible for as much as 74% of gas exchange impairment. Atelectasis may even persist into the postoperative period, causing a decrease in PaO₂ and an increase in the potential for accumulation and systemic translocation of bacteria. Use of a low FiO₂ (40% to 50%) is common in human anesthesia and decreases the degree of atelectasis and intrapulmonary shunting, resulting in improved gas exchange. Involving a low concentration (30% to 50%) of inspired oxygen have been performed in many veterinary species, revealing improvements in ventilation and decreases in intrapulmonary shunting. Use of air-oxygen mixtures in dogs and cats improves lung aeration and atelectasis as assessed via CT.

In anesthetized, mechanically ventilated horses, gradually increasing the FiO₂ to > 90% improves oxygenation, compared with the immediate use of 100% oxygen. When managing isoflurane anesthesia in horses, hypopventilation and ventilation perfusion mismatch might be improved through the use of oxygen-air mixtures. Clinically, the reluctance to use gases other than 100% oxygen might be attributable to occasional hypoxemia (PaO₂ < 60 mm Hg) that can develop, despite delivering 100% oxygen. Additionally, most machines designed for large animal anesthesia are equipped with only an oxygen flow meter and are not equipped to deliver air-oxygen mixtures. The objective of the study reported here was to evaluate whether the use of 50% inspired oxygen versus > 95% oxygen would alter the respiratory pattern of spontaneously breathing isoflurane-anesthetized horses by increasing ventilation and generating a more constant ventilatory rhythm. A second objective was to examine whether the use of 50% inspired oxygen would affect gas exchange over time by measuring the rate of change in PaO₂ - PaO₂ as well as PaO₂ and SaO₂. The hypothesis was that horses breathing 50% inspired oxygen would have an increase in minute ventilation, a decrease in PaCO₂, a less irregular ventilatory rhythm, and a smaller rate of change in PaO₂ - PaO₂ over time than when breathing > 95% oxygen.

Materials and Methods

Animals—Eight horses (6 geldings and 2 mares) were used in the study. Ages ranged from 6 to 20 years (median, 10 years), and body weight ranged between 480 and 630 kg (median, 526 kg). Breeds included Quarter Horse (n = 5), Thoroughbred (2), and Appaloosa (1). All horses had various musculoskeletal diseases but were judged to be of physical status I of the American Society of Anesthesiologists classification system on the basis of physical examination and CBC results. Food and water were made available to the horses until the morning of the study. The study protocol was approved by the Kansas State University Institutional Animal Care and Use Committee.

Study protocol—A random number table was used to assign horses to the order in which they would undergo each of 2 anesthetic sessions, 7 days apart: maintenance of isoflurane anesthesia with an inspired oxygen concentration of 50% or maintenance with an inspired oxygen concentration of > 95%. In preparation, a 14-gauge, 7.5-cm catheter was inserted in the right jugular vein of each horse for drug and fluid administration. The large animal anesthetic breathing circuit was to be used in the study was preloaded with 2.5% isoflurane in 100% or 60% oxygen, depending on treatment assignment. Twenty minutes prior to the beginning of anesthesia by circulation of 2.5% isoflurane in 60% oxygen (and 40% nitrogen) or 2.5% isoflurane in 100% oxygen until the desired concentration was achieved. Preloading with isoflurane was considered necessary to attain the desired ETISO within the first 5 minutes of anesthesia. Preloading the breathing circuit with 60% oxygen was necessary to allow for partial denitrogenation of the horse’s lungs and to attain a stable inspired concentration of oxygen of 50% or > 95% within those first 5 minutes. Oxygen and isoflurane concentrations were measured with a previously calibrated multiparameter monitoring system. The breathing system was then sealed until horses were connected to the breathing circuit Y-piece.

Xylazine hydrochloride (1.0 mg/kg, IV) was administered to the horses 5 minutes prior to anesthetic induction with diazepam (0.05 mg/kg, IV) and ketamine hydrochloride (2.2 mg/kg, IV). They were endotracheally intubated with a cuffed endotracheal tube (internal diameter, 26 mm) and then hoisted and positioned in dorsal recumbency on a padded surgery table. Additional ketamine hydrochloride (0.2 mg/kg, IV) was administered when horses were deemed insufficiently anesthetized for hoisting.

Once a horse had been positioned, the endotracheal tube was connected to the preloaded anesthesia breathing circuit. Anesthesia was maintained with isoflurane (ETISO 1.5 %), and the inspired oxygen concentration was maintained at 50% or > 95% after the initial 5 minutes necessary to attain the desired oxygen concentration and ETISO.

Horses breathed spontaneously throughout the study, with no intervention even during prolonged periods of apnea. Carrier gas flow was 8 L/min for the full 90 minutes of inhalation anesthesia in each session. Control of inspired oxygen concentration was achieved.

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by adjusting a calibrated air-oxygen blender. Lactated Ringer's solution was administered IV at 5 mL/kg/h.

When the 90-minute session concluded, acepromazine maleate (0.006 mg/kg, IV) was administered and horses were nasotracheally intubated. As horses recovered from anesthesia, oxygen was administered via a cather inserted to the distal tip of the nasotracheal tube at a rate of 15 L/min. After the first anesthetic session, horses were allowed to recover unassisted in a recovery stall equipped with a rapidly inflating-deflating air pillow. After the second session, horses were euthanized because of the aforementioned musculoskeletal diseases.

Instrumentation and data collection—A 20-gauge, 5-cm catheter coated with a nonstick polymer was inserted percutaneously into a mandibular artery for direct arterial blood pressure recording and collection of blood samples. The blood pressure transducer was positioned at the point of the shoulder.

A multichannel recorder and data acquisition system were used to digitize and record arterial pressure waveforms, ECG tracings, and respiratory flows. The multiparameter monitor was used to display gas concentrations and pulse oximetry readings. Information derived from these systems was noted frequently, and gas concentrations and oxygen hemoglobin saturation were recorded at predetermined data acquisition periods. Calibration was accomplished with manufacturer-recommended gases.

Respiratory flow rate was measured with a calibrated pneumotachograph attached to the air inlet-outlet of a bag-in-a-barrel system. The pneumotachograph was connected to a differential pressure transducer interfaced with the data acquisition system. Before each anesthetic session, equipment calibration was performed, including measurement of air flow through the pneumotachograph via a precision rotameter. Integration of the flow signal for tidal volume determination was checked by use of a 7-L calibration syringe. The ventilatory rhythm (respiratory rate and apnea duration) of each horse was observed and recorded during the entire anesthetic session. Periods of apnea were defined as the interval between the end of expiration when flow was no longer being generated and the point at which flow was restarted during the inspiratory phase of the following respiratory cycle.

Arterial pressure waveforms, ECG tracings, and respiratory flows were monitored continuously and recorded every 5 minutes for the first 30 minutes and every 10 minutes for the remaining 60 minutes, with the moment a horse was connected to the preloaded breathing circuit designated as time 0. Care was taken to ensure that by 5 minutes after time 0, the target inspired oxygen concentration and the ET \(_{\text{ISO}}\) of 1.5% had been attained. A cather extending through the lumen of the endotracheal tube to the distal end was used for evaluation of end-tidal and inspiratory gases. Mixed expired gas (\(\text{P} \text{CO}_2\) and \(\text{P} \text{O}_2\) \(\text{P} \text{EO}_2\)) samples were collected through a multiport sampling cather extending the entire length of the corrugated expiratory breathing hose of the anesthetic breathing circuit. The multiorifice sampler was constructed of small-bore tubing (outer diameter, 2.35 mm; inner diameter, 1.25 mm). The distal end of the tubing was sealed. Nine small orifices 15 cm apart were created along its length (143 cm). Mixed expired gas samples were collected continuously during expiratory flow in three 20-mL aliquots over 3 consecutive respiratory cycles into a 60-mL syringe. All gas analysis was performed with a calibrated gas analyzer.

Collected cardiovascular and respiratory data analyzed included systolic, diastolic, and mean arterial blood pressures; heart rate; inspiratory and expiratory peak flow; inspiratory and expiratory duration; tidal volume; respiratory frequency; and respiratory rhythm. Tidal volume was automatically integrated from the expiratory flow signal. Respiratory and anesthetic gas measurements included end tidal \(\text{CO}_2\), \(\text{P} \text{CO}_2\), \(\text{P} \text{O}_2\), \(\text{P} \text{EO}_2\), \(\text{ET} \text{ISO}\) and fractional inspired isoflurane concentration.

Arterial blood samples were aspirated from the arterial catheter into heparinized syringes during 3 consecutive respiratory cycles 15, 30, 60, and 90 minutes after time 0. Samples were immediately sealed and analyzed for \(\text{P} \text{AO}_2\), \(\text{P} \text{ACO}_2\), \(\text{pH}\), \(\text{S} \text{AO}_2\), \(\text{PCV}\), and total protein concentration. All gas values were corrected to the concurrent rectal temperature, which was measured with a calibrated thermistor.

Minute ventilation, \(V_{d}/V_{t}\), \(\text{P} \text{AO}_2\), \(\text{P} \text{ACO}_2\), \(\text{P} \text{O}_2\) - \(\text{P} \text{O}_2\), and rate of change in \(\text{P} \text{AO}_2\) - \(\text{P} \text{O}_2\) over time were calculated. Minute ventilation was calculated by multiplying tidal volume by respiratory rate and correcting to body temperature and barometric pressure, saturated with water vapor. Respiratory rate and tidal volume were measured over a 5-minute period to minimize measurement bias. Physiologic dead space ratio was calculated on the basis of the following equation:

\[
V_{d}/V_{t} = (\text{P} \text{CO}_2 - \text{P} \text{EO}_2)/\text{P} \text{CO}_2
\]

Partial pressure of alveolar oxygen was calculated on the basis of the alveolar gas equation:

\[
\text{P} \text{AO}_2 = \text{P} \text{ACO}_2 - \text{P} \text{O}_2 \times (((\text{P} \text{O}_2 - \text{P} \text{EO}_2)/\text{P} \text{EO}_2)
\]

The partial pressure difference between alveolar and arterial oxygen was calculated as \(\text{P} \text{AO}_2\) minus \(\text{P} \text{AO}_2\).

Statistical analysis—Summary statistics are reported as mean ± SD. General linear mixed models were developed to test the effectiveness of the treatment between the 2 anesthetic sessions for all response variables. The P value obtained from the F test was used to determine whether a difference existed in the mean responses between the treatments. Changes in values of response variables over time were also compared between treatments through performance of effects-level contrast. Multiple tests were performed to compare responses at each time point during each anesthetic session, with the response occurring at 5 minutes after horses were connected to the anesthetic circuit. A Tukey adjustment was used to adjust the resulting P values to account for multiple comparisons. The Student t test was also performed at each time point to identify differences in mean response values between...
the treatments at those specific time points. Values of P < 0.05 were considered significant for all analyses.

Results

No significant differences in values of any cardiovascular variable were identified between the 2 treatments (50% and > 95% oxygen inspiration) at any point. Mean ± SD heart rates for the 90-minute anesthetic sessions were 39.2 ± 4.2 beats/min and 38.9 ± 3.6 beats/min for horses breathing 50% and > 95% oxygen, respectively. Mean arterial blood pressure steadily decreased between 5 and 40 minutes after horses were connected to the anesthetic circuit (time 0), followed by a steady increase between 40 and 90 minutes after time 0 for both treatments. Hypotension, defined as mean arterial blood pressure < 60 mm Hg, was evident during both treatments between 20 and 70 minutes after time 0, with no significant difference between the treatments. There were no significant differences in PCV, blood total protein concentration, blood pH, or rectal temperature between the treatments.

No significant difference in minute ventilation was observed between the 2 treatments once the target inspired oxygen concentration and the ETSo, of 1.5% were attained. A greater minute ventilation was observed during the first 5 minutes after time 0 when the lower inspired oxygen concentration was used. Hypoventilation of statistically similar degrees was identified with both treatments. The mean PACO2 was 51.9 ± 9.5 mm Hg and 57.5 ± 10.8 mm Hg for horses breathing 50% and > 95% oxygen, respectively, and these values were not significantly different. There were also no significant differences in tidal volume, respiratory rate, inspiratory and expiratory duration, inspiratory and expiratory peak flow, or any other respiratory values between treatments at any time point (Table 1).

The respiratory flow rate was higher than at 5 minutes after connection to the anesthesia circuit for both treatments at all subsequent measurement points. On the other hand, the treatments were not different after 5 minutes when both treatments were used simultaneously, and values of any cardiac-vascular variables were identified between the 2 treatments. The mean Heart rate was 39.2 ± 4.2 beats/min and 38.9 ± 3.6 beats/min for horses breathing 50% and > 95% oxygen, respectively.

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<table>
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<th>Variable</th>
<th>Oxygen (%)</th>
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<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
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<tr>
<td>Peak inspiratory flow (L/s)</td>
<td>50</td>
<td>4.1 ± 1.2</td>
<td>4.3 ± 1.9</td>
<td>5.1 ± 1.4</td>
<td>5.7 ± 3.1*</td>
<td>5.7 ± 2.5</td>
<td>5.9 ± 3.6</td>
<td>5.8 ± 2.4</td>
<td>6.1 ± 3.2</td>
<td>6.0 ± 2.7</td>
<td>6.6 ± 4.0</td>
<td>6.7 ± 3.9</td>
<td>6.8 ± 3.5</td>
<td>6.8 ± 3.7*</td>
</tr>
<tr>
<td>Inspiratory duration (s)</td>
<td>&gt; 95</td>
<td>2.0 ± 0.8</td>
<td>3.0 ± 1.0</td>
<td>2.8 ± 1.1</td>
<td>2.7 ± 1.2</td>
<td>2.6 ± 1.1</td>
<td>2.7 ± 1.3</td>
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<td>2.6 ± 1.2</td>
<td>2.5 ± 1.0</td>
<td>2.5 ± 0.8</td>
<td>2.4 ± 0.6</td>
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<td>2.5 ± 0.6</td>
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<tr>
<td>Peak expiratory flow (L/s)</td>
<td>&gt; 95</td>
<td>5.7 ± 9.3</td>
<td>4.4 ± 1.4</td>
<td>8.3 ± 4.4</td>
<td>8.4 ± 1.4*</td>
<td>8.6 ± 1.4*</td>
<td>8.7 ± 1.4</td>
<td>8.8 ± 1.5</td>
<td>8.3 ± 1.5</td>
<td>8.2 ± 1.5*</td>
<td>8.2 ± 1.5</td>
<td>8.2 ± 1.5*</td>
<td>8.2 ± 1.5</td>
<td>8.2 ± 1.5*</td>
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<tr>
<td>Expiratory duration (s)</td>
<td>&gt; 95</td>
<td>0.9 ± 0.2</td>
<td>1.2 ± 0.3</td>
<td>1.6 ± 0.2*</td>
<td>1.4 ± 0.4</td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.3</td>
<td>1.5 ± 0.4</td>
<td>1.3 ± 0.4</td>
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<tr>
<td>Tidal volume (L)</td>
<td>&gt; 95</td>
<td>5.2 ± 2.4</td>
<td>7.5 ± 3.1</td>
<td>9.3 ± 3.6</td>
<td>10.5 ± 2.5</td>
<td>9.9 ± 2.1</td>
<td>10.1 ± 1.8</td>
<td>11.0 ± 2.5</td>
<td>9.6 ± 2.1</td>
<td>10.0 ± 3.0</td>
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<td>Respiratory rate (breaths/min)</td>
<td>&gt; 95</td>
<td>5.4 ± 3.0</td>
<td>3.1 ± 1.6</td>
<td>2.7 ± 1.8</td>
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<td>2.9 ± 1.0</td>
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<td>Minute ventilation (L/min)</td>
<td>&gt; 95</td>
<td>5.4 ± 3.0</td>
<td>3.1 ± 1.6</td>
<td>2.7 ± 1.8</td>
<td>2.2 ± 0.8</td>
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<td>2.8 ± 1.0</td>
<td>2.9 ± 1.0</td>
<td>3.0 ± 0.9</td>
<td>3.0 ± 0.9</td>
<td>3.1 ± 0.9</td>
<td>3.8 ± 1.0</td>
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*Values differ significantly (P < 0.05) between 5 minutes after horses were connected to the circle rebreathing system and the indicated time point.

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<tr>
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<th>60</th>
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<td>50</td>
<td>7.34 ± 0.05</td>
<td>7.33 ± 0.05</td>
<td>7.35 ± 0.05</td>
<td>7.37 ± 0.08</td>
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<td>SPO2 (%)</td>
<td>&gt; 95</td>
<td>7.32 ± 0.05</td>
<td>7.31 ± 0.06</td>
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<tr>
<td>SaO2 (%)</td>
<td>&gt; 95</td>
<td>90.9 ± 2.2*</td>
<td>90.4 ± 2.1*</td>
<td>88.8 ± 6.1</td>
<td>85.8 ± 14.3</td>
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<tr>
<td>PaO2 (mm Hg)</td>
<td>&gt; 95</td>
<td>93.3 ± 2.2</td>
<td>93.3 ± 2.8</td>
<td>92.8 ± 2.6</td>
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<tr>
<td>PaCO2 (mm Hg)</td>
<td>&gt; 95</td>
<td>98.6 ± 1.5</td>
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<tr>
<td>Vp/pf</td>
<td>&gt; 95</td>
<td>51.6 ± 8.5</td>
<td>54.5 ± 8.8</td>
<td>51.4 ± 8.1</td>
<td>50.8 ± 12.5</td>
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</table>

*Value differs significantly (P < 0.05) from value for other treatment at same time point. SPO2 = Oxygen saturation as measured by pulse oximetry.

Table 1—Mean ± SD values of respiratory variables in 8 healthy adult isoflurane-anesthetized horses breathing 50% and > 95% oxygen at various points (minutes) after connection to a preoxygenated circle anesthetic system.

Table 2—Mean ± SD values of arterial blood gas variables in 8 healthy adult isoflurane-anesthetized horses inspiring 50% and > 95% oxygen at various points (minutes) after connection to a preoxygenated circle anesthetic system.
hand, inspiratory duration was longer than at the 5-min-
ute point at all subsequent points when horses breathed
50% oxygen. No differences in inspiratory duration were
detected at any point when horses breathed > 95% oxy-
gen. Each horse had its own ventilatory pattern that was
consistent for both treatments from 10 to 90 minutes after
ime 0. Apneic periods were horse dependent and ranged
in duration from 2 seconds to 4 minutes.

Values for PaO₂ and SaO₂ were significantly higher at all
measurement points when horses were anesthetized with
isoflurane in > 95% oxygen than when 50% oxygen was
used (Table 2). Mean values for PaO₂ were 203.0 ± 113.3
mm Hg and 77.8 ± 19.7 mm Hg, respectively. Those for SaO₂
were 98.7 ± 1.4% and 92.9 ± 3.6%, respectively. A greater
PaO₂ - PaO₂ was evident with the use of > 95% oxygen than
with 50% oxygen. Mean PaO₂ - PaO₂ was 380.5 ± 113.9 mm
Hg for > 95% oxygen and 194.8 ± 31.6 mm Hg for 50% oxygen.
No difference was evident in the rate of change in
PaO₂ - PaO₂ in V̇/V̇ between the 2 treatments.

Discussion

Air-oxygen mixtures are used routinely as an an-
esthetic delivery gas in human medicine. Use of a low
FiO₂ (30% to 50%) in humans decreases the likelihood of
intraoperative atelectasis and improves oxygenation
during the postoperative recovery period. In con-
trast, air-oxygen mixtures are not commonly used dur-
ing inhalation anesthesia in veterinary practice, but a
low FiO₂ has been used during anesthesia of dogs, cats,
and horses in experimental studies. Advantages of the use of a low FiO₂ demonstrated clinically and
experimentally include improvements in minute ven-
tilation and gas exchange and a decrease in ventilation
perfusion mismatch in horses. Advantages include
improvements in minute ventilation and gas exchange and a decrease in ventilation perfusion mismatch in horses and cats, resulting in better gas exchange.

In the study reported here, ventilatory characteristics,
oxgenation, and rate of change in PaO₂ - PaO₂ were
analyzed in spontaneously breathing horses anesthe-
tized with isoflurane at 2 oxygen concentrations (30%
and > 95%). Minute ventilation was different during
the initial 5 minutes when horses were connected to
the breathing circuit, with higher minute ventilation
evident when the lower concentration of inspired oxy-
gen was administered. Breath holding was not observed
during the first 5 minutes, and respiratory rate was
higher during this period than during any subsequent
time point for both oxygen concentrations. The reason
for higher minute ventilation with the 50% concentra-
tion is unclear, and because PaO₂ and SaO₂ were not
measured, one can only speculate as to the cause.

A difference in minute ventilation shortly after in-
duction of inhalation anesthesia in horses with different
inspired oxygen concentrations has not been reported.
A previous study revealed a change in ventilation on
the basis of PaCO₂ measurements, but that study did not
involve collection of arterial blood samples for blood
gas analysis until 15 minutes after horses had been
connected to the breathing circuit. Consequently, it is
possible differences existed but were missed. In another
study, researchers observed a higher minute ventila-
tion and respiratory rate as well as a decrease in PaCO₂
in horses breathing 21% oxygen versus > 95% oxygen 5
minutes after induction using total IV anesthesia. This
increase in minute ventilation was maintained until the
horses began to receive > 95% oxygen (15 minutes after
anesthetic induction). In our study, no significant dif-
ference between treatments was observed after the ini-
tial 5 minutes of inhalation anesthesia. The clinical im-
portance of this observation can be argued because horses
breathing > 95% oxygen were able to reach the desired
ETISO at the same time as horses breathing 50% oxygen;
therefore, the lower minute ventilation appeared adequate
for the interval between injectable anesthetic administra-
tion and isoflurane anesthesia.

Ventilatory characteristics varied markedly among
the horses of the present study. Because each horse was
used as its own control, this allowed for assess-
ment of individual breathing patterns twice. Ventilatory
rhythm for each horse, which was characterized by
respiratory rate and duration of apnea, was similar
for both oxygen concentrations. Ventilatory rhythm
can be inhalant dependent. For example, isoflurane-
anesthetized horses have a breathing pattern that can
be characterized as a low respiratory rate and an irreg-
ular rhythm, whereas halothane-anesthetized horses
have a higher and more regular respiratory rate. Our
findings suggested that the irregular respiratory pat-
tern associated with isoflurane anesthesia is no differ-
ent when a low versus high FiO₂ is used. Respiratory
patterns for individual horses were continuous and re-
petitive, beginning 10 minutes after connection to the
breathing circuit and persisting until the end of the
anesthetic session when breathing isoflurane (ETISO,
1.5%) in 50% or > 95% oxygen.

In 1 horse, 4-minute periods of apnea were con-
sistently observed during the 90-minute session with
both treatments. Such prolonged periods of apnea
can be challenging for anesthetists to manage because
maintenance of an adequate anesthetic depth in such
circumstances can be difficult and hypercarbia and
hypoxemia can result. Prolonged apneic periods were
accompanied by a steady decrease in oxygen hemog-
lobin saturation as measured by pulse oximetry until
respiration resumed. For the horse with the 4-minute
periods of apnea, an additional arterial blood sample
was collected for blood gas analysis during one of the
episodes to identify the degree of hypercarbia or hy-
poxemia. The results from this additional arterial blood
gas analysis revealed moderate to severe hypercarbia
(PaCO₂, 71.7 mm Hg) but not hypoxemia (PaO₂, 80.0
mm Hg), despite apnea for a period of > 2 minutes.
However, the associated blood sample might not have
been representative of the eventual PaO₂ of this horse
when the duration of apnea reached 4 minutes. This
blood sample was collected while the horse was breath-
ing > 95% oxygen. We did not repeat the arterial blood
gas measurements during an apneic period when the
same horse was breathing 50% oxygen, and it is pos-
sible that such an apneic period while the horse was
breathing the lower oxygen concentration would have
resulted in hypoxemia. The irregular respiratory rate
and long periods of apnea in some horses of our study
emphasizes the need to have a mechanical ventilator
available when isoflurane is used as the inhalation an-

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esthetic, not only to avoid hypercarbia and hemoglobin desaturation but also to allow constant delivery of the volatile agent and to assist in maintaining an adequate anesthetic depth.

Administration of a high FiO₂ (> 95%) has been associated with a greater degree of atelectasis formation in humans, horses, dogs, and cats than when a lower fraction (< 50%) is used.9,16-19 Anesthetized horses develop severe intrapulmonary shunting as a result of collapsed alveoli (atelectasis), leading to a large PAO₂ - PaO₂.2,3,9,23 Atelectasis formation results from loss of pulmonary surfactant, airway compression, and absorption of gas distal to closed airways.24 Absorption atelectasis develops in the presence of intermittent airway closure (low ventilation-to-perfusion ratio zones), followed by absorption of alveolar gas into the capillary blood, resulting in alveolar collapse. Use of 30% to 50% inspired oxygen in humans decreases the likelihood of absorption atelectasis by avoiding the complete collapse of intermittently closed alveoli through the use of an accompanying inert or poorly absorbed gas such as nitrogen.24

A large PAO₂ - PaO₂ was observed in all horses for both oxygen concentrations assessed in the present study. A decrease in PAO₂, PaO₂ can reflect a decrease in intrapulmonary shunting, but it is not an accurate indicator of that shunting because PaO₂, PaO₂ is affected by many physiologic factors such as administered fraction of inspired oxygen, hemoglobin concentration, and arterial-venous oxygen content difference.25 Other variables have been proposed to quantify the degree of oxygen transfer or intrapulmonary shunting, including PaO₂/ FiO₂, PaO₂/PaO₂, and (PAO₂ - PaO₂)/PaO₂, with all of these being inaccurate estimates to various extents.26 The most accurate method to measure oxygen transfer and pulmonary function is estimation of the degree of intrapulmonary shunting through collection and analysis of mixed venous blood as well as arterial blood.26 A pulmonary arterial catheter was not used in our study; therefore, the degree of intrapulmonary shunting could not be estimated and we could not conclude that the use of 50% inspired oxygen resulted in a decrease in intrapulmonary shunting. In another study,26 horses anesthetized with isoflurane in 50% oxygen and mechanically ventilated also had a lower PaO₂ - PaO₂ than did horses breathing > 95% oxygen, but when the shunt fraction was measured, no difference was found between the 2 oxygen concentrations.27 These findings reemphasize the inaccuracy of PaO₂ - PaO₂, as a predictor of intrapulmonary shunting and call into question the impact of compression versus absorption atelectasis formation in horses.

The high PAO₂ - PaO₂ detected shortly after anesthetic induction with both oxygen concentrations used supports previous studies14,15,26 of atelectasis development early in the course of anesthesia in horses. Early development of intrapulmonary shunting during equine anesthesia is caused primarily by compression atelectasis and is more severe in horses positioned in dorsal versus lateral recumbency.2 In the study reported here, a progressive increase in PAO₂ - PaO₂ was noticed during both anesthetic sessions, but the rate of increase during the 90 minutes of anesthesia did not differ between oxygen concentrations used. The increase in PAO₂ - PaO₂ over time suggested a continued increase in intrapulmonary shunting with both oxygen concentrations, possibly because of a progression in atelectasis. Breathing the 50% oxygen concentration should, in concept, have resulted in a lower rate of increase in PAO₂ - PaO₂ if absorption atelectasis were the predominant problem after the initial compression atelectasis. It is possible that the horses were not anesthetized long enough. Laterally recumbent horses anesthetized with halothane in 30% or 85% oxygen had a significant increase in PAO₂ - PaO₂ while breathing the higher versus lower oxygen concentration, but the increase was detected only after 120 minutes of anesthesia in another study.2 It is also possible that the chosen FiO₂ was not optimal. We chose to evaluate only 2 oxygen concentrations, and it could be that the FiO₂ of 50% was still too high. Additional studies are warranted to identify the ideal FiO₂ for dorsally recumbent horses. Lastly, the compression atelectasis generated in horses during dorsal recumbency is generally of such severity that absorption atelectasis becomes inconsequential. Evaluation of horses in lateral recumbency, during which compression atelectasis is less severe,3 may yield different effects of changes in PAO₂ - PaO₂ over time.

Use of > 95% oxygen resulted in a significantly higher SaO₂ and PaO₂ in the present study. Most horses breathing 50% oxygen had a hemoglobin saturation > 90%. Hypoxemia was noticed in 12.5% of all measurements obtained, with half of the hypoxic events developing in 1 particular horse. No hypoxemia was evident when > 95% oxygen was used. Another study27 also resulted in a lower PaO₂ with 50% versus > 95% inspired oxygen treatment but revealed no difference in SaO₂ or oxygen delivery. A low PaO₂ can be acceptable as long as saturation and oxygen delivery are maintained. The difference in saturation between the other study27 and our study may have been attributable to instant initiation of mechanical ventilation in the other study rather than the spontaneous ventilation in our study. Mechanical ventilation in horses has been associated with an improvement in PaO₂ when initiated immediately after anesthetic induction.29

Other ventilatory modalities have been attempted to decrease atelectasis, increase gas exchange, and improve PaO₂ in horses. Recruitment maneuvers, although effective in horses, require the repetitive use of high pressures (60 to 80 cm H₂O), and PEEP needs to be instituted to keep the recruited alveoli open.30 In humans, recruitment maneuvers with 100% oxygen but without PEEP result in closing of the alveoli shortly after the maneuver, followed by resorption of gas and return of atelectasis.13 Disadvantages associated with repeated recruitment maneuvers and PEEP are barotrauma and a decrease in cardiac output.31,32 In humans, use of a low FiO₂ (40%) after recruitment maneuvers results in a diminished and slower reappearance of atelectasis.13 Whether the same phenomenon occurs in horses is unknown. Opening and maintenance of collapsed alveoli through use of 40% to 50% oxygen may yield some of the benefits associated with PEEP without the decrease in cardiac output.

Postanesthetic atelectasis may persist in humans for up to 4 days and can result in an increase in the probability of postoperative hypoxemia and pulmonary infection.13,14 Use of air-oxygen mixtures decreases the
amount of atelectasis, improves gas exchange, and decreases the degree of postoperative hypoxia. In horses recovering from anesthesia, hypoxemia reportedly develops when they are in lateral recumbency, even with administration of supplemental oxygen. We did not measure postoperative PaO₂, so the effects of a low FiO₂ during anesthetic recovery remain unknown in horses.

The study horses were hypotensive for variable durations. Administration of drugs, such as ephedrine or dobutamine, for the treatment of hypotension during equine anesthesia can increase cardiac output. An increase in cardiac output increases oxygen delivery, resulting in increased mixed venous oxygen tension. The increase in mixed venous oxygen tension subsequently decreases the venous admixture, ultimately increasing PaO₂. We elected not to treat horses for any periods of hypotension to avoid increases in PaO₂ originating from changes in cardiac output instead of improvement in gas exchange.

Use of 50% oxygen and nitrogen as the carrier gas did not significantly change the ventilatory characteristics in the isoflurane-anesthetized horses in our study. Horses maintained a low respiratory rate with a regularly irregular ventilatory rhythm with both inspired oxygen concentrations. The ventilatory rhythm was continuous and repetitive at the selected ETISO, and a high PaO₂ - PaO₂ existed with an equal rate of change over time, independent of inspired oxygen concentration used. Overall, the findings suggested that the use of 50% inspired oxygen does not improve ventilatory rhythm or gas exchange and increases the risk of hypoxemia in spontaneously breathing horses during isoflurane anesthesia. Should 50% inspired oxygen be used in horses, adequate monitoring and the capacity for mechanical ventilation are highly recommended.

References


