Effect of administration of propofol and xylazine hydrochloride on recovery of horses after four hours of anesthesia with desflurane

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Objective—To compare characteristics of horses recovering from 4 hours of desflurane anesthesia with and without immediate postanesthetic IV administration of propofol and xylazine.

Animals—8 healthy horses (mean ± SEM age, 6.6 ± 1.0 years; mean body weight, 551 ± 50 kg).

Procedures—Horses were anesthetized twice. Both times, anesthesia was induced with a combination of xylazine hydrochloride, diazepam, and ketamine hydrochloride and then maintained for 4 hours with desflurane in oxygen. Choice of postanesthetic treatment was randomly assigned via a crossover design such that each horse received an IV injection of propofol and xylazine or saline (0.9% NaCl) solution after the anesthetic episode. Recovery events were quantitatively and qualitatively assessed. Venous blood samples were obtained before and after anesthesia for determination of serum creatine kinase activity and plasma propofol concentration.

Results—Anesthetic induction and maintenance were unremarkable in all horses. Compared with administration of saline solution, postanesthetic administration of propofol and xylazine resulted in an increased interval to emergence from anesthesia but improved quality of recovery-related transition to standing. Compared with administration of saline solution, administration of propofol also delayed the rate of decrease of end-tidal concentrations of desflurane and carbon dioxide and added to conditions promoting hypoxemia and hypoventilation.

Conclusions and Clinical Relevance—Propofol and xylazine administered IV to horses after 4 hours of desflurane anesthesia improved the quality of transition from lateral recumbency to standing but added potential for harmful respiratory depression during the postanesthetic period. (Am J Vet Res 2009;70:956–963)

In horses, recovery from general anesthesia is potentially life threatening, even when horses are healthy and anesthetic management and surgery are considered routine. Injuries commonly occur during recovery when the horse regains at least partial consciousness and attempts to stand but is too uncoordinated to be successful.

Strategies to facilitate recovery without injury are limited in number and extent of application and yield inconsistent results. For example, a common strategy to facilitate a desired, smooth, coordinated emergence from inhalation anesthesia and an atraumatic return to a standing posture is administration of a short-acting sedative at the end of general anesthesia. Xylazine hydrochloride or another α2-adrenergic receptor agonist is commonly administered near or at the end of general anesthesia. Xylazine hydrochloride or another α2-adrenergic receptor agonist is commonly administered near or at the end of general anesthesia to promote a more gradual recovery of consciousness and thereby delay the horse’s attempt to stand while providing more time for elimination of anesthetic from the lungs.14 Results of an experimental study5 in which horses were anesthetized with isoﬂurane for 90 minutes and treated with a 30-minute IV infusion of xylazine and ketamine hydrochloride afterward indicated that postanesthetic treatment did not
result in improved quality of recovery, compared with the quality of recovery in horses that received no postanesthetic treatment.

Results of a study of propofol in equids suggested that an excitement-free recovery from anesthesia is possible. We have reported similarly promising findings for anesthetic protocols that include propofol. Results of the study reported here was to compare characteristics of horses recovering from 4 hours of desflurane anesthesia with and without immediate postanesthetic IV administration of propofol and xylazine. Desflurane was selected for maintenance of anesthesia because results of studies in other animal species suggest more rapid pulmonary elimination of this inhalation anesthetic at the end of anesthesia, compared with that of other contemporary inhalation anesthetics. Because, to the authors’ knowledge, pulmonary elimination of desflurane has not been evaluated in horses, another objective was to characterize the rate of decrease in alveolar (end-tidal) desflurane concentration during recovery from anesthesia.

Materials and Methods

Animals—Eight healthy university-owned horses (6 geldings and 2 mares) were used in the study. Mean ± SEM age was 6.6 ± 1.0 years (range, 4 to 12 years), and mean body weight was 551 ± 50 kg. Breeds included Thoroughbred (n = 4), Quarter Horse (1), Paint (1), Standardbred (1), and Hanoverian-cross (1). Food (but not water) was withheld for approximately 12 hours prior to each anesthetic episode. The study protocol was approved by the university’s animal use and care committee.

Experimental protocol—Each horse was anesthetized twice, with at least 1 month between anesthetic episodes. Xylazine hydrochloride (1 mg/kg, IV) was administered 5 minutes before induction of anesthesia in a padded stall routine used for anesthetic recovery. General anesthesia was induced with diazepam (0.025 mg/kg, IV) and ketamine hydrochloride (2 mg/kg, IV). Each horse was endotracheally intubated, positioned in left lateral recumbency on a thick pad on a transfer cart, and moved into the laboratory for continuation of general anesthesia. The endotracheal tube was attached to a standard large-animal circle anesthetic system, and general anesthesia was then maintained from this point with desflurane delivered in O₂ (6 L/min). By 1 hour after the diazepam and ketamine injection, the alveolar (end-tidal) desflurane concentration was maintained at 9.7% (equivalent to 1.2 × MAC) for the remainder of the 4-hour anesthetic episode (ie, 3 hours of a constant dose of desflurane).

End-tidal desflurane concentration was determined by withdrawal of a respiratory gas sample through a catheter positioned in the tracheal tube lumen and measurement of the sample with an anesthetic analyzer. Inspired and end-tidal respiratory gases were collected in a similar manner and measured for O₂ and CO₂ concentration by use of calibrated Beckman gas analyzers or an automated mass-spectrometer system. Nasopharyngeal temperature was monitored via a calibrated thermistor and lactated Ringer’s solution was infused via a left saphenous vein catheter at a rate of 3 mL/kg/h. A catheter was percutaneously placed in the right facial or carotid artery and connected to a calibrated Beckman gas analyzer.

Recovery from inhalation anesthesia—A balanced crossover design was used. Horses were assigned to receive IV administration of propofol (0.75 mg/kg) or an equivalent volume of saline (0.9% NaCl) solution after each anesthetic episode, such that each horse received each postanesthetic treatment once. The order of treatments was determined a priori such that 4 horses would receive saline solution first, whereas the other 4 would receive propofol first. After 3.5 hours of anesthesia, spontaneous ventilation was resumed and the horses, still connected to the anesthetic breathing circuit and maintained on desflurane at 1.2 × MAC, were moved to the same padded recovery stall in which anesthesia was induced. Each horse was positioned on the floor of the dimly lit recovery stall in left lateral recumbency. At 4 hours after anesthetic induction with diazepam and ketamine, inhalation anesthesia was abruptly halted by disconnecting the endotracheal tube from the breathing circuit. Horses remained intubated until they started to vigorously chew on the tube.

Five minutes after disconnection of the breathing circuit, propofol (0.75 mg/kg) or an equivalent volume of saline solution (placebo) was administered as an IV bolus delivered from 60-mL syringes over 3 minutes. Eight minutes after the circuit was disconnected (3 minutes after the loading dose of propofol was administered), a continuous rate IV infusion of propofol (0.125 mg/kg/min) and xylazine (0.03 mg/kg/min) was initiated for 15 minutes in horses that had already received propofol. The 2 drugs were administered separately but simultaneously via a calibrated IV infusion pump (propofol) and a syringe pump (xylazine). Because of the large volume of propofol necessary, the calculated amount of propofol was transferred from individual vials to a new, sterile 500-mL fluid bag for the timed infusion delivery.

Whenever a period of apnea exceeding 2 minutes was detected during propofol administration, drug delivery was stopped and intermittent positive-pressure ventilation was briefly applied (1 to 2 breaths/min) via a demand valve powered by 100% O₂. Observation of clinical signs of sedation and return of spontaneous ventilation guided
continuation of drug delivery. The delay in drug delivery was usually brief (ie, 30 to 120 seconds). All horses received the entire calculated dose of postanesthetic drugs. Only the duration of drug delivery varied and was based largely on any onset of apnea. At the end of the infusions, each spontaneously breathing horse was allowed to recover without assistance while directly observed. Care was taken to avoid any type of stimulus (eg, auditory, visual, or tactile) that might promote premature arousal in the awakening, recumbent horse, with the exception of monitoring for vital signs and obtaining blood and expired gas samples early in the recovery phase.

During the early phase of recovery from inhalation anesthesia, end-tidal respiratory gas samples were obtained by hand via a glass syringe from a catheter positioned within the endotracheal tube lumen and the time-related changes in end-tidal desflurane and CO₂ concentrations were measured until signs of arousal were detected. To avoid confounding these measurements, supplemental O₂ was not administered until after the aforementioned expiratory gas measurements, at which time the inspired air was supplemented with O₂ via endotracheal insufflation (O₂ flow, 15 L/min).

Times of all recovery-related events were recorded as minutes from disconnection of the breathing circuit. Additional recordings included intervals to the following events: first detection of nystagmus; first movement of eyelid, ear, limb, and head; first attempt at head lift, swallowing, and chewing; first detection of shivering; first move to sternal and standing postures; first standing; and extubation. The number of attempts to obtain sternal and standing postures was also recorded. Quality of the horse’s movement from a sternal to standing posture was independently subjectively graded by at least 3 of the unblinded investigators according to a scheme described elsewhere, and the results are reported as the mean of these individual opinions.

Collection and analysis of blood samples obtained during the recovery period—A sample of jugular venous blood was collected from each horse 30 to 60 minutes prior to the induction of anesthesia for measurement of serum creatinine kinase activity. Within 1.5 hours after sample collection, serum was harvested and frozen in sealed vials until analyzed (usually the same day but no more than 3 days after collection). For the same purpose, a blood sample was also obtained at the end of inhalation anesthesia, immediately after horses stood, and at 1 day following each anesthetic episode. When the anesthetic circuit was disconnected (end of inhalation anesthesia), arterial and jugular venous blood samples were collected in heparinized syringes for measurement of blood gas partial pressures, pH, and plasma propofol concentration. Similarly, blood samples were collected when possible at 10, 17, and 28 (for analysis of plasma propofol concentration only) minutes after propofol administration began (equivalent to 15, 22, and 33 minutes after the anesthetic circuit was disconnected) and at between 1 to 3 minutes and 15 minutes after the horse stood. Following blood collection, syringes were capped and immediately placed in ice pending analysis or, more commonly, submitted for immediate blood gas measurements. Plasma for propofol analysis was separated from blood samples via centrifugation within 1 hour after blood collection and was frozen at −70°C until analyzed later by one of the investigators (LKM).

Method of analysis of plasma propofol concentration—Plasma propofol concentrations were determined via high-performance liquid chromatography with fluorescence detection by use of a modified version of a method described elsewhere. The equipment consisted of an automated system with a C-18 column and guard column (150 × 4.6 mm; 5-µm particle size) maintained at 40°C. The mobile phase consisted of 0.025% trifluoroacetic acid and acetonitrile at a flow rate of 1.5 mL/min. Propofol and the internal standard thymol were eluted in isocratic conditions of 40% (trifluoroacetic acid) and 60% (acetonitrile), followed by an increase of acetonitrile to 90% from 5 to 6.5 minutes after injection and equilibration to initial conditions for 6.5 minutes.

Analysts were detected at an excitation wavelength of 275 nm, and emission was detected at 310 nm. Calibrants were prepared in plasma from blood samples of unmedicated horses at concentrations of 0.05, 0.1, 0.25, 0.5, 1, 2, 4, and 8 µg/mL. The calibrants and experimental samples were treated identically, except that calibrants were assayed once, whereas experimental samples were assayed in duplicate. One hundred microliters of each calibrant or experimental sample was vortex mixed with 200 µL of water. Proteins were precipitated by adding 500 µL of acetonitrile containing 0.1 µg/mL of thymol, followed by centrifugation and injection of 50 µL of the resulting supernatant onto the column. The limit of quantitation, defined as the concentration at which the accuracy and precision were within 80% to 120% when samples were reanalyzed on different days, was 0.05 µg/mL. At a nominal propofol concentration of 0.8 µg/mL, the mean recovery of propofol from plasma was 74% (range, 69% to 77%). At nominal propofol concentrations of 0.94 and 6.4 µg/mL, the accuracy of the method was 98% and 99%, respectively, whereas the relative SD was 1% and 4%, respectively.

Statistical analysis—Data were summarized and are expressed as mean ± SEM. Subjectively derived recovery scores are summarized as median and range of values. Inferential analyses were performed with statistical software. Comparisons of data that were normally distributed were analyzed by use of the paired t test or repeated-measures ANOVA, followed when appropriate by a Tukey test. Data that were not normally distributed were analyzed with Friedman repeated-measures ANOVA on ranks, followed when appropriate by the Bonferroni nonparametric multiple comparison correction. A value of P < 0.05 was considered significant for all analyses.

Results

Anesthetic induction was unremarkable in all horses. Doses of drugs administered for anesthetic induction did not differ in relation to choice of postanesthetic treatment (Table 1). While horses were anesthetized, ventilation and arterial blood pressure were maintained within the limits previously defined. Dobutamine was administered for varying periods during anesthesia in only 3 situations (involving 3 horses and both types of postanesthetic treat-
ments). Mean ± SEM pharyngeal temperature during anesthesia was 36.5 ± 0.2°C.

Table 1—Mean ± SEM doses (mg) of drugs administered for induction of general anesthesia in 8 horses anesthetized twice (with at least 1 month between anesthetic episodes), with immediate postanesthetic IV administration of propofol and xylazine hydrochloride (treatment) or an equivalent volume of saline (0.9% NaCl) solution (placebo).

<table>
<thead>
<tr>
<th>Drug</th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xylazine</td>
<td>550 ± 21</td>
<td>547 ± 18</td>
</tr>
<tr>
<td>Diazepam</td>
<td>13.7 ± 0.5</td>
<td>13.6 ± 0.4</td>
</tr>
<tr>
<td>Ketamine</td>
<td>1,101 ± 43</td>
<td>1,095 ± 36</td>
</tr>
</tbody>
</table>

Mean preanesthetic body weight of horses was 551 ± 21 kg and 546 ± 19 kg for the first and second procedures, respectively.

Five minutes after disconnection of the anesthetic breathing circuit, propofol (0.75 mg/kg) or saline solution was administered as an IV bolus delivered from 60-mL syringes over 3 minutes. Eight minutes after the circuit was disconnected (3 minutes after the loading dose of propofol was administered), a continuous rate IV infusion of propofol (0.125 mg/kg/min) and xylazine (0.03 mg/kg/min) was initiated for 15 minutes in horses that had already received propofol.

The mean loading dose of propofol was 410 ± 13 mg, and the mean total dose of propofol administered during the 15-minute IV infusion following the loading dose was 1,012 ± 120 mg. The mean dose of xylazine coadministered during the propofol constant rate infusion was 239 ± 13 mg.

Cardiorespiratory responses during recovery from desflurane—Results of cardiovascular and respiratory measurements made before induction of general anesthesia and during desflurane recovery without and with propofol and xylazine were summarized (Table 2). In some situations, measurements were not made for personnel safety reasons or to avoid confounding a horse's behavior during recovery. Administration of propofol and xylazine was associated with hypercapnia during the recumbent phase of anesthesia and during desflurane recovery without and with propofol and xylazine coadministered during the propofol constant rate infusion (43 mg, and the mean total dose of propofol administered during the 15-minute IV infusion following the loading dose was 1,012 ± 120 mg. The mean dose of xylazine coadministered during the propofol constant rate infusion was 239 ± 13 mg.

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Table 2—Mean ± SEM values of cardiovascular and respiratory variables in 8 horses before and at various points during anesthetic recovery and during desflurane anesthesia, with immediate postanesthetic IV administration of propofol and xylazine (treatment) or an equivalent volume of saline solution (placebo).

<table>
<thead>
<tr>
<th>Variable, by treatment</th>
<th>HR (beats/min)</th>
<th>RR (breaths/min)</th>
<th>MAP (mm Hg)</th>
<th>Arterial blood pH</th>
<th>Arterial base balance (mEq/L)</th>
<th>PCV (%)</th>
<th>Plasma protein concentration (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before anesthesia</td>
<td>15 minutes after DC</td>
<td>20 to 25 minutes after DC</td>
<td>5 minutes after standing</td>
<td>15 minutes after standing</td>
<td>Before DC</td>
<td>15 minutes after DC</td>
</tr>
<tr>
<td>Placebo</td>
<td>38 ± 2</td>
<td>33 ± 1</td>
<td>33 ± 1 (7)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Treatment</td>
<td>38 ± 3</td>
<td>35 ± 1</td>
<td>32 ± 2 (7)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Placebo</td>
<td>20 ± 2</td>
<td>4 ± 1</td>
<td>8 ± 1</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Treatment</td>
<td>19 ± 2</td>
<td>4 ± 1</td>
<td>6 ± 2</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Placebo</td>
<td>ND</td>
<td>67 ± 6</td>
<td>111 ± 9</td>
<td>109 ± 6 (7)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Treatment</td>
<td>ND</td>
<td>67 ± 6</td>
<td>111 ± 9</td>
<td>109 ± 6 (7)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Placebo</td>
<td>94 ± 5</td>
<td>113 ± 14</td>
<td>76 ± 7 (4)</td>
<td>ND</td>
<td>85 ± 3 (7)</td>
<td>ND</td>
<td>85 ± 2</td>
</tr>
<tr>
<td>Treatment</td>
<td>98 ± 4</td>
<td>102 ± 13</td>
<td>66 ± 10</td>
<td>78 ± 15 (7)</td>
<td>84 ± 6</td>
<td>ND</td>
<td>82 ± 5</td>
</tr>
<tr>
<td>Placebo</td>
<td>74 ± 2</td>
<td>75 ± 2</td>
<td>49 ± 3 (4)</td>
<td>ND</td>
<td>49 ± 2 (7)</td>
<td>ND</td>
<td>47 ± 1</td>
</tr>
<tr>
<td>Treatment</td>
<td>73 ± 3</td>
<td>75 ± 3</td>
<td>67 ± 7*</td>
<td>67 ± 7* (7)</td>
<td>57 ± 6*</td>
<td>ND</td>
<td>49 ± 1</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.42 ± 0.01</td>
<td>7.27 ± 0.01</td>
<td>7.39 ± 0.01*</td>
<td>ND</td>
<td>7.39 ± 0.01 (7)</td>
<td>ND</td>
<td>7.41 ± 0.01 (7)</td>
</tr>
<tr>
<td>Treatment</td>
<td>7.41 ± 0.01</td>
<td>7.26 ± 0.02</td>
<td>7.31 ± 0.03*</td>
<td>7.30 ± 0.03 (7)</td>
<td>7.38 ± 0.01 (7)</td>
<td>ND</td>
<td>7.41 ± 0.01 (7)</td>
</tr>
<tr>
<td>Placebo</td>
<td>3 ± 1</td>
<td>6 ± 1</td>
<td>4 ± 1 (4)</td>
<td>ND</td>
<td>4 ± 1 (7)</td>
<td>ND</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>Treatment</td>
<td>3 ± 1</td>
<td>5 ± 1</td>
<td>5 ± 1</td>
<td>5 ± 1 (7)</td>
<td>5 ± 1</td>
<td>ND</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Placebo</td>
<td>43 ± 2</td>
<td>45 ± 3</td>
<td>42 ± 2 (4)</td>
<td>ND</td>
<td>45 ± 3 (7)</td>
<td>ND</td>
<td>41 ± 3</td>
</tr>
<tr>
<td>Treatment</td>
<td>44 ± 2</td>
<td>45 ± 1</td>
<td>39 ± 1</td>
<td>37 ± 1 (7)</td>
<td>39 ± 1</td>
<td>ND</td>
<td>35 ± 1</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate the number of horses when different from 8.

*Values within a time category are significantly (P < 0.05) different.

DC = Disconnection of endotracheal tube from anesthetic circuit (ie, end of desflurane administration), while horses were still in lateral recumbency. HR = Heart rate. ND = Not determined. RR = Respiratory rate. MAP = Mean arterial blood pressure.

See Table 1 for remainder of key.
infusion. When apnea was detected, intermittent positive-pressure ventilation was briefly administered (1 to 2 breaths/min) until spontaneous ventilation resumed (ie, within 2 to 5 minutes). For all measurements conducted during recovery from desflurane with propofol, heart rate ranged from a mean of 29 ± 1 beats/min to 38 ± 1 beats/min, and this response did not differ from values obtained during recovery without propofol. Similarly, mean respiratory rate (not including apneic periods) ranged from 3 ± 1 breaths/min to 9 ± 2 breaths/min and mean arterial blood pressure ranged from 66 ± 5 mm Hg to 117 ± 7 mm Hg. Values for heart rate, respiratory rate, and mean arterial blood pressure were generally lower during the early recovery period than in the later recumbent period or after horses stood; however, these differences were not significant.

Elimination of desflurane and CO₂—The end-tidal concentrations of desflurane and CO₂ at various times relative to their end-tidal concentrations when horses were disconnected from the anesthetic circuit (ie, the end of desflurane administration) were summarized (Figure 1). Pulmonary elimination of desflurane in the absence of propofol and xylazine treatment was rapid. By 3 minutes after the anesthetic breathing circuit was disconnected, the end-tidal concentration had decreased from 9.7% (equivalent to 1.2 × MAC14) to 2% (ie, approx 0.2 × MAC), by approximately 6 minutes, it was < 1%. Administration of propofol and xylazine noticeably slowed the pulmonary elimination of desflurane and CO₂.

Recovery behavior—Intervals to detection of various events characterizing the behavior of horses as they recovered from desflurane anesthesia without and with propofol and xylazine treatment were summarized (Table 3). Recovery from desflurane in the absence of propofol and xylazine was rapid, and a subjective score ranging from good to excellent quality was typically assigned; 5 of the 8 recoveries were judged excellent.

Three horses had brief bouts of so-called head-slapping or frantic behavior as they attempted to rise to a sternal position, which, in our experience, are moves commonly observed in horses recovering from inhalation anesthesia. When these behaviors were observed, it was typically during the early period of active attempts to move to a sternal position and the instances of head slapping were few in number (1 to 3 episodes) and brief. However, some of the moves were forceful and potentially harmful (although not in the present study). Following the head slapping, the horses lay quietly in lateral recumbency for a moment and then proceeded to sternal and standing positions in a quiet, usually favorable, calm manner.

The potentially traumatic head slaps observed during recovery from desflurane anesthesia without postanesthetic propofol and xylazine administration were not typically observed after propofol and xylazine treatment. Rather, after administration of propofol and xylazine, the horses typically lifted their heads off the floor and, if unable to assume a sternal position, returned their heads to a resting lateral position in a highly controlled manner (similar to rising from an unsedated recumbency). A slow, well-controlled and coordinated rise to standing, even when horses were positioned awkwardly within the recovery stall (eg, near a corner), was characteristic of recoveries following administration of propofol and xylazine (7/8 were judged excellent). Regardless of whether horses were treated with propofol and xylazine, ataxia was not commonly detected when horses stood, and within 4 to 6 minutes of standing, horses were generally interested in leaving and judged able to safely leave the recovery

Table 3—Mean ± SEM interval (minutes) to first observation of recovery characteristics in 8 horses recovering from desflurane anesthesia after disconnection from circle anesthetic system, with immediate postanesthetic IV administration of propofol and xylazine (treatment) or an equivalent volume of saline solution (placebo).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystagmus</td>
<td>5.1 ± 0.9</td>
<td>30.3 ± 5.5</td>
</tr>
<tr>
<td>Blink</td>
<td>7.1 ± 1.4</td>
<td>39.5 ± 3.9</td>
</tr>
<tr>
<td>Move ear</td>
<td>14.6 ± 3.5</td>
<td>48.5 ± 4.9</td>
</tr>
<tr>
<td>Move limb</td>
<td>13.8 ± 1.2</td>
<td>45.9 ± 3.8</td>
</tr>
<tr>
<td>Move head</td>
<td>9.5 ± 1.0</td>
<td>45.0 ± 3.3</td>
</tr>
<tr>
<td>Lift head</td>
<td>13.2 ± 1.2</td>
<td>49.0 ± 3.2</td>
</tr>
<tr>
<td>Swallow</td>
<td>7.9 ± 1.1</td>
<td>42.7 ± 2.5</td>
</tr>
<tr>
<td>Chew</td>
<td>17.8 ± 1.7</td>
<td>56.4 ± 3.8</td>
</tr>
<tr>
<td>Shiver</td>
<td>10.8 ± 1.1</td>
<td>42.4 ± 6.4</td>
</tr>
<tr>
<td>First move to sternal posture</td>
<td>14.1 ± 1.2</td>
<td>51.7 ± 3.2</td>
</tr>
<tr>
<td>Extubation</td>
<td>21.1 ± 2.1</td>
<td>62.3 ± 3.3</td>
</tr>
<tr>
<td>First move to stand</td>
<td>22.6 ± 2.2</td>
<td>70.3 ± 6.5</td>
</tr>
<tr>
<td>Stand</td>
<td>29.4 ± 2.0</td>
<td>73.6 ± 6.7</td>
</tr>
</tbody>
</table>

*Values are significantly (P < 0.05) different between treatments. See Table 1 for remainder of key.
stall and walk back to their barn stall. After returning to their stalls, all horses were interested in food. Despite minimal or no detected decrease in body temperature, shivering was characteristic of all horses recovering from desflurane. In some horses, the shivering was so intense that had the horses been less conscious and, in particular, more ataxic they likely would have fallen back to a recumbent position. However, shivering was not detected in 3 horses when treated with propofol and xylazine and the intensity of shivering appeared to be less in the other 5, compared with the intensity in untreated horses.

Before induction of anesthesia, the serum activity of creatine kinase for all horses was within the reference range (119 to 287 U/L) of the analyzing laboratory (Table 4). There were no differences in values following desflurane anesthesia that could be attributed to propofol and xylazine treatment.

Plasma propofol concentration—The lower limit of plasma propofol quantitation was 0.05 µg/mL. Propofol was not detected in any plasma from blood samples obtained before induction of anesthesia. At 15 minutes after horses were disconnected from the desflurane anesthetic system (10 minutes after the bolus IV administration and 2 minutes after the constant rate infusion of propofol began), the mean plasma propofol concentration was 4.34 ± 0.36 µg/mL. At 22 minutes after disconnection (17 minutes after IV administration of propofol and xylazine began and at the end of the constant rate infusion of propofol and xylazine), the mean plasma propofol concentration was 4.04 ± 0.39 µg/mL. Mean values at various points after IV administration of propofol and xylazine were discontinued were as follows: 10 minutes afterward (33 minutes after disconnection from the desflurane anesthetic system), 0.40 ± 0.05 µg/mL; 51 ± 7 minutes afterward (5 minutes after horses stood), 0.11 ± 0.02 µg/mL; and 61 ± 7 minutes afterward (15 minutes after horses stood), 0.07 ± 0.01 µg/mL.

Discussion

The large size of horses and the nature of their responses to threatening circumstances often contribute to injury and occasionally even death during recovery from anesthesia. Although anesthetic and recovery management of horses is improving, there remains a need to more reliably facilitate that recovery to ensure a more consistent, favorable outcome for anesthetized horses. A desirable recovery from anesthesia is more than simply ensuring that horses resume a standing posture; the manner in which the posture is gained is equally or more important.

The objective of the present study was to evaluate whether the combination of desflurane and propofol would yield a safe and consistent recovery for horses, which are often fractious when emerging from inhalation anesthesia. For various reasons, we assumed that inhalation anesthetics will continue to be the most widely used drugs for managing anesthesia for > 1 hour, and therefore, any recovery protocol developed should account for the recovery time and species-specific behavior associated with elimination of the anesthetic. The choice to evaluate desflurane as opposed to other inhalation anesthetics was because its low blood solubility results in rapid elimination from the body and recovery times are short. Results of studies of anesthetic recovery profiles of rats, pigs, and humans strongly correspond with reports of anesthetic recovery time and behavior of desflurane-anesthetized horses that were treated with or without commonly administered anesthetic adjuvant drugs such as xylazine, diazepam, and ketamine. Also important to our decision was that the anesthetic potency (MAC) and cardiorespiratory effects of desflurane are known for ponies and horses, and this information was compatible with the study goals.

In the present study, anesthetic management of horses with desflurane was unremarkable and values of objective measurements of cardiorespiratory function were similar to those reported elsewhere. Observations made during anesthetic recovery of horses were also qualitatively similar to those we have made in the past. Recovery times generally averaged slightly longer in the present study, compared with recovery times in our earlier study. This difference was attributed to typical interindividual variation and the residual sedative influence of anesthetic induction drugs. The rate of decrease of end-tidal desflurane concentration measured in the present study was greater than that reportedly measured in horses after halothane and isoflurane anesthesia.

These data confirmed our expectations regarding the rate of recovery as based on blood solubility of desflurane and anesthetic recovery behavior in smaller species and accounted for the rapid return to various recovery events and standing (Table 3). The decrease in end-tidal desflurane concentration may have been influenced, although probably only slightly if at all, by a residual effect of the induction drugs. The lack of traumatic recovery was further supported by minimal or nonexistent changes in serum creatine kinase activity measured after anesthesia and recovery. Except for the predictable hypercapnia at the end of desflurane anesthesia (spontaneous ventilation) and at the earliest stage of recovery and the accompanying mild hypoxemia during the recumbency phase of recovery, values of cardiovascular and respiratory variables during recovery from anesthesia were unremarkable.

Our goal for a desirable recovery from anesthesia was a smooth, atraumatic transition from lateral recumbency to a sternal posture, followed by a smooth, coordinated,
careful rise to standing; such motions are similar to the natural transition from lateral recumbency to standing in an awake, unmedicated horse. Once standing, horses should remain quietly standing or, if ambulatory, should be so without ataxia or stumbling. In an attempt to achieve this goal, we elected to smooth the transition from desflurane anesthesia to standing in horses by temporarily sedating the recovering horses with propofol.

Propofol is a potent sedative and injectable anesthetic that has been used in human and veterinary medicine for several years. Specific characteristics that make this drug useful are a short duration of action, minimal cumulative effect with repeated administration, rapid recovery from sedation or anesthesia, and, in humans, good immediate postanesthetic psychomotor performance. Indeed, from earliest investigations of propofol in horses, including our own, the consistent high quality of recovery following its use in otherwise unmedicated horses made this drug stand out from other sedatives and injectable and inhalation anesthetics.

We considered it important to administer an adrenergic receptor agonist (xylazine) with the propofol. Reasoning to do so included the need to prevent or obscure the often unpredictable myoclonus and limb paddling that sometimes accompanies propofol use in otherwise unmedicated or lightly sedated horses. Also, because the technique was being investigated for ultimate clinical use, it was considered appropriate to add an analgesic component. An opioid was not chosen as an adjuvant drug for several reasons. First, opioids do not have potent sedative properties in horses, particularly when opioids are used alone and in clinical dosages. In addition, there is evidence to suggest that opioids do not prevent the sporadic muscular stiffness or limb paddling occasionally associated with propofol administration. Finally, because opioids can cause behavioral arousal, opioid use could have confounded the results in the present study. Consequently, an adrenergic receptor agonist was selected instead. Xylazine was chosen because of its short duration of action. The dosage used was that which we believed would yield a small additional effect of sedation without resulting in ataxia when the recovering horse attempted to stand or instability immediately after standing.

Use of the propofol-xylazine combination after horses were disconnected from the circle anesthetic system and cessation of desflurane administration had desirable and undesirable (but largely predictable and modifiable) effects. Movements throughout recovery from lateral through sternal and to standing positions were more consistent and uniformly coordinated when propofol and xylazine were administered than when these drugs were not administered. There was little to no ataxia at the time of standing. In most situations, horses treated with propofol and xylazine simply stood up as if quietly arising from a period of wakeful recumbency. The frantic, forceful, fractious attempts to stand that are often evident in horses after inhalation anesthesia were absent. The often traumatic head-smacking or head-hanging behavior that can occur with an uncoordinated attempt to attain a sternal posture was not seen. In addition, fewer propofol-treated horses had the intense shivering that was evident when they were recovering from desflurane anesthesia without propofol, and the shivering that did occur was less forceful than that which occurred without propofol administration.

The respiratory depression that accompanied propofol administration in the horses of the present study was expected. Signs included hypoventilation, hypoxemia, and in the extreme, apnea. The magnitude of effect appeared to be related to the rate of propofol administration. Accordingly, the rate of administration and timing of propofol bolus administration and infusions should be modified slightly in future studies. The pulmonary elimination characteristics of desflurane determined in the present study will be helpful in this regard. The continued hypoventilation associated with administration of propofol and xylazine altered the rate of change of end-tidal CO_{2} and desflurane concentrations over time and contributed to a greater degree and duration of hypoxemia than was detected when propofol and xylazine were not administered. Accordingly, keeping equipment for mechanical ventilation nearby in the event of drug-induced apnea and providing O_{2} supplementation of inspired air would be required for clinical application of this recovery technique.

Not surprisingly, administration of propofol and xylazine during the anesthetic recovery period resulted in an increased duration of recumbency in horses, compared with the duration of recumbency when the drugs were not administered. However, there was no evidence that this additional duration was detrimental because recovery quality in horses when treated with propofol and xylazine appeared superior to that when they were not treated. Although serum creatine kinase activity in treated versus untreated horses was significantly increased at 1 day after propofol administration, the magnitude of this increase was judged of little or no biological importance.

It is important to mention that prolongation of immobile recumbency on a firm surface during recovery from anesthesia has the potential to result in neuropathy or myopathy in horses. Indeed, we expected an increase in complications with more profound cardiopulmonary depression in the recovery period or a substantial increase in the duration of immobile recumbency when propofol was administered. An untested condition in which this might be anticipated is the substitution of isoflurane for desflurane.

c. AnaSed, Akorn Inc, Decatur, Ill.
d. Diazepam, Hospira Inc, Lake Forest, Ill.

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