**Effects of postanesthetic sedation with romifidine or xylazine on quality of recovery from isoflurane anesthesia in horses**

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**Objective**—To test the hypothesis that postanesthetic sedation with romifidine would dose-dependently improve recovery quality of recovery from isoflurane anesthesia in horses more than postanesthetic sedation with xylazine.

**Design**—Prospective, randomized, blinded clinical trial.

**Animals**—101 healthy adult horses examined at the University of California-Davis Veterinary Medical Teaching Hospital from 2007 to 2009.

**Procedures**—Horses were sedated with xylazine, and anesthesia was induced with guaifenesin, diazepam, and ketamine via a standardized drug protocol. Anesthesia for surgical or diagnostic procedures was maintained with isoflurane in oxygen for 1 to 4 hours. At the end of anesthesia, horses were moved to a padded stall for recovery. Once the breathing circuit was disconnected and the patient was spontaneously breathing, either xylazine (100 or 200 µg/kg [45 or 91 µg/lb]) or romifidine (10 or 20 µg/kg [4.5 or 9.1 µg/lb]) was administered IV. Objective patient, surgical, and anesthesia data were recorded. Subjective visual analog scale (VAS) scores of recovery quality were assigned by a single individual who was unaware of the treatment received. A stepwise linear regression model was used to correlate patient and procedure factors with the VAS score.

**Results**—Painful procedures, longer anesthesia times, and the Arabian horse breed were associated with poorer VAS scores. Adjustment for these factors revealed an improved VAS recovery score associated with the use of a romifidine dose of 20 µg/kg.

**Conclusions and Clinical Relevance**—In healthy adult horses anesthetized with isoflurane for > 1 hour, the results of this study supported the use of 20 µg of romifidine/kg, IV, rather than lower romifidine doses or xylazine, for postanesthetic sedation to improve recovery quality. (*J Am Vet Med Assoc* 2013;242:533–539)

Equine anesthesia is associated with an extraordinarily high incidence of perioperative mortality. One prospective study involving 41,824 cases in 142 different clinics in 19 different countries found a 2.1% mortality rate for all horses within 7 days of general anesthesia. If only anesthetics for noncolic procedures were considered, the perianesthetic mortality rate was still nearly 1 in 100 cases. Approximately one-third of these deaths were due to postanesthetic fractures and myopathies, for which recovery quality likely played a contributing role.

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**ABBREVIATION**

<table>
<thead>
<tr>
<th>VAS</th>
<th>Visual analog scale</th>
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Horses may exhibit dysphoria or excitement during recovery from inhalation anesthesia. Poor recoveries are characterized by repetitive head banging on the ground, paddling limb movements, lunging, rolling, flopping, falling, knuckling, uncoordinated attempts to stand, or a combination of these behaviors.2,3 These behaviors resemble emergence delirium in humans in which patients scream, kick, thrash, or exhibit altered mental status during the first 30 minutes of anesthetic recovery.4 Although long-term consequences in human patients are unclear, emergence delirium in horses may predispose to cuts, abrasions, bruises, or, more seriously, fractures, tendon or ligament tears, myopathies, and death.

The speed of anesthetic recovery, types of anesthetic drugs used, presence of postoperative pain, and patient age and temperament may all contribute to emergence delirium in people. In prospective, randomized, blinded trials in children, α2-adrenoreceptor agonists have been shown to decrease the incidence and severity of postanesthetic emergence delirium, presumably as a consequence of the sedative and analgesic properties of...
these drugs.\textsuperscript{6–7} Similarly, postanesthetic sedation using \( \alpha_2 \)-adrenoreceptor agonists in horses prolongs recovery time but improves recovery quality from isoflurane or sevoflurane, compared with saline controls.\textsuperscript{6–11}

However, which \( \alpha_2 \)-adrenoreceptor agonist and what dose should be used to best improve recovery quality have not been established. Compared with xylazine, the \( \alpha_2 \)-adrenoreceptor agonist romifidine is approximately 10 times as potent, has a longer duration of clinical effect, and produces less ataxia at doses that similarly reduce responses to tactile stimulation.\textsuperscript{12} As a result, romifidine might provide analgesia and tranquilization during anesthetic recovery while minimizing \( \alpha_2 \)-adrenoreceptor agonist–mediated ataxia that could otherwise negate some of the recovery benefits. Santos et al\textsuperscript{13} reported that low, equipotent doses of xylazine or romifidine improved recovery quality from isoflurane anesthesia, but the investigators found no difference between agents. However, only 6 horses were studied, parametric statistical tests were used to analyze a multidimensional composite score, and other contributors to anesthetic recovery were not factored in the model to help reduce the error sum-of-squares in the analysis. Hence, analytic methods and sample size may have precluded detection of a drug effect. Bartman, et al\textsuperscript{10} also reported no difference in recovery quality from postanesthetic administration of an equipotent dose of either xylazine or romifidine. Yet in addition to other recovery effects not being controlled for in the statistical analysis, horses that received xylazine postoperatively received xylazine for premedication, whereas horses that received romifidine postoperatively received romifidine for premedication. Since romifidine has a longer duration of action than xylazine,\textsuperscript{13} the contribution of preanesthetic \( \alpha_2 \)-adrenoreceptor agonist to postanesthetic sedation for short procedures would be greater for romifidine than for xylazine. Hence, the cumulative postanesthetic \( \alpha_2 \)-adrenoreceptor agonist plasma concentration-to-potency ratio between agents may not have been equivalent.

The purpose of the study reported here was to determine whether \( \alpha_2 \)-adrenoreceptor agonist dose, agent (xylazine or romifidine), or both improve anesthetic recovery quality in an equine clinical trial that used a standardized anesthetic protocol. To increase the likelihood of detecting a drug effect, we simultaneously determined whether other signalment, anesthesia, or surgical factors may explain some of variability in patient anesthetic recovery quality. For example, preanesthetic temperament of a horse influences anesthetic recovery quality and time to first head lift; since temperament is influenced by horse breed and age, these objective measurements were simultaneously examined. Anesthetic washout during anesthetic recovery is influenced by sedative administration, which decreases minute alveolar ventilation,\textsuperscript{14} total anesthetic time, anesthetic depth, and use of an oxygen demand valve in recovery; these factors were also included for study since faster washout could affect recovery times and qualities. Moreover, because a given postanesthetic sedative-analgesic drug and dose may produce variable effects in an individual horse on the basis of temperament, presence or absence of pain, and concurrent doses of maintenance anesthetics, it was necessary that a study design account for these possible cofactors.

We hypothesized that horses sedated with romifidine would have better recovery scores than horses sedated with xylazine. We also hypothesized that increasing the dose of the postanesthetic \( \alpha_2 \)-adrenoreceptor agonist would significantly improve recovery quality, assuming that the drug did not also worsen postanesthetic ataxia.

**Materials and Methods**

This study was designed as a prospective, randomized, blinded clinical trial using client-owned horses that were examined at the Veterinary Medical Teaching Hospital at the University of California-Davis from 2007 to 2009. Drugs and doses used in this study all fell within accepted hospital standards of care for equine postanesthetic sedation. This protocol was approved by the Animal Use and Care Committee at the University of California-Davis.

Horses included in this study had no evidence of cardiovascular, respiratory, hepatic, renal, or neurologic disease on the basis of physical and hematologic evaluation and met the criteria established by the American Society of Anesthesiologists classification system for a physical status of I to II.\textsuperscript{14} In addition, horses needed to be 2 years of age or older, weigh between 270 and 680 kg (594 and 1,496 lb), and require general anesthesia for an elective procedure lasting 1 to 4 hours. Horses undergoing ocular procedures were excluded since these animals generally require special recovery techniques to minimize risks of disruption of the repair. Finally, horses undergoing a laparotomy were excluded because of special concerns about analgesia management and differences in postoperative morbidity and mortality rates, compared with those in the general equine anesthetic population.\textsuperscript{3} To achieve a type I error rate of 5%, power of 80%, and regression effect size (Cohen's \( F^2 \))\textsuperscript{15} of 0.25 with a model that could contain up to 16 variables, a minimum of 91 horses would be required for this study. One hundred horses were enrolled to allow for slightly greater variability than initially estimated.

Some horses initially enrolled in this study did not complete it. A priori criteria for censoring included intraoperative reassessment of patient needs with a decision to assist recovery or to administer nonstudy systemic or regional opioid analgesics. Additionally, patients that received any injectable anesthetics within the final 30 minutes of inhaled anesthesia were also removed from the study. Opioids\textsuperscript{6,17} and ketamine\textsuperscript{18,19} may independently affect recovery quality or recovery times in horses sedated with \( \alpha_2 \)-adrenoreceptor agonists; thus administration of these drugs potentially could have increased response variability within the xylazine or romifidine treatments.

By means of a random number table, horses were allocated to receive 1 of 4 treatments: xylazine (100 \( \mu \)g/kg [45 \( \mu \)g/lb], IV), xylazine (200 \( \mu \)g/kg [91 \( \mu \)g/lb], IV), romifidine (100 \( \mu \)g/kg [45 \( \mu \)g/lb], IM), or romifidine (200 \( \mu \)g/kg [91 \( \mu \)g/lb], IM).
A syringe containing 1 mL/kg (0.45 mL/lb) plus another syringe containing 2 mL/kg (0.91 mL/lb) for each patient; one syringe contained the study drug, and the other contained saline (0.9% NaCl) solution, which allowed the investigators to be blinded to drug dose since both would be simultaneously administered to the patient. The study drug was delivered to the anesthetist by a different pharmacy technician who was also unaware of the assigned treatment. A sealed envelope containing the study drug and saline solution were administered as an IV bolus. The recovery stall doors were then closed, and recovery was video recorded and observed from outside the stall.

Objective measures of recovery such as total anesthesia time (time from anesthetic induction until circuit disconnection), use of the oxygen demand valve, time between circuit disconnection until first spontaneous movement, number of repetitive head bangs on the floor, time from circuit disconnection until first successful sternal recumbency, time from disconnection until final standing, and number of attempts to stand were recorded by the attending anesthesiologist. Subjective recovery measures including the VAS score, evaluation of ataxia, and limb-paddling severity (none, mild, moderate, or severe) were always made by the same veterinary anesthesiologist either during anesthetic recovery or during review of the video recording. The VAS was scored by marking a 100-mm scale, with 0 indicating a poor recovery quality and 100 indicating an excellent or ideal recovery; the VAS equaled the distance between the mark and 0 in millimeters. Treatment codes for study horses were not revealed until after all patients had been studied and all subjective measurements were completed.

Continuous data were summarized as mean ± SD, median, and range. Binary data, such as anesthesia for a painful procedure and demand valve use, were coded as 1 if the event occurred and 0 if it did not. Binary variables were used to code N-1 categorical variables with the remaining category serving as the reference group. To examine the effect of patient sex, separate variables for gelding and stallion were created, with mare serving as the reference group. Breed effects were examined by creating separate variables for Arabian, Quarter Horse, and Thoroughbred horses; all other breeds were combined as the reference group that consisted largely of various warmblood breeds. For the recovery drugs, binary variables for 200 µg/kg of xylazine, 10 µg/kg of romifidine, and 20 µg/kg of romifidine were created, and the 100 µg/kg xylazine dose was used for reference. A multivariate stepwise least squares linear regression model was created with statistical software to test for correlation between the VAS score and the following variables: age, weight, sex, breed, anesthesia for a painful procedure, total anesthetic time, end-tidal isoflurane concentration at the time of circuit disconnection, use of an oxygen demand valve after circuit disconnection, time between circuit disconnection and first spontaneous movement, time between circuit disconnection and standing recovery (total recovery time), and postanesthetic recovery drug and dose. Continuous data that were not normally distributed, as evidenced by Wilk-Shapiro tests and visual inspection of probability plots, were mathematically transformed to a variable with a normal distribution for use in the regression analysis. A value of $P \leq 0.05$ was used as the criterion for variable inclusion in the forward stepwise model and for variable exclusion in the backward stepwise model.

To understand factors that influence an overall recovery VAS score, Spearman correlation coefficients
were used to measure separately the association between VAS and limb paddling severity, ataxia severity, number of repetitive head slaps on the floor, the number of attempts to sternal recumbency, and the number of attempts to stand. For all tests, a value of \( P \leq 0.05 \) was considered significant.

**Results**

Complete data were available for 101 horses. Summary data by drug treatment group were summarized (Table 1). Fifty-nine of the horses enrolled were of Arabian, Quarter Horse, or Thoroughbred breeds. Of the remaining horses classified as other, there were 25 various warmblood breeds, 4 Morgans, 3 Paints, 2 Quarter Horse/Thoroughbred crosses, and 1 each of Andalusian, Appaloosa, Mustang, Palamino, Paruvian Paso, pony, Standardbred, and Trakehner breeds. Most elective procedures (44%) involved endoscopy of joints, bursae, or tendon sheath, although orchidectomies (20%) and nonpainful diagnostic imaging procedures (11%) were also common (Table 2).

There were no anesthetic complications associated with anesthetic induction. All but 1 horse required IV dobutamine administration for blood pressure support during anesthetic maintenance. Alveolar-to-arterial \( P_{O_2} \) gradients were increased in many patients during anesthesia, but only 4 had a measured \( P_{O_2} \) between 60 and 80 mm Hg, and no horses experienced more severe hypoxemia. Of the former, 3 horses were assigned the 100 \( \mu \)g/kg xylazine dose for recovery and had VAS scores of 12, 58, and 76. The remaining horse was assigned to the 200 \( \mu \)g/kg xylazine treatment group and had a \( VAS \) of 23. The low number of affected patients in this study precluded further inferences pertaining to hypoxemia. No other complications during anesthetic maintenance were reported.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cases</th>
<th>Painful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthroscopy (1 joint)</td>
<td>32</td>
<td>Yes</td>
</tr>
<tr>
<td>Arthroscopy (2 joints)</td>
<td>5</td>
<td>Yes</td>
</tr>
<tr>
<td>Arthroscopy (3 joints)</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Bone or hoof débridement</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Burscopy</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Castration</td>
<td>9</td>
<td>Yes</td>
</tr>
<tr>
<td>Castration + umbilical hernia</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Cryptorchid castration</td>
<td>10</td>
<td>Yes</td>
</tr>
<tr>
<td>CT</td>
<td>9</td>
<td>No</td>
</tr>
<tr>
<td>CT + angiography</td>
<td>3</td>
<td>No</td>
</tr>
<tr>
<td>CT + angiography + débridement</td>
<td>1</td>
<td>Yes</td>
</tr>
<tr>
<td>Desmotomy or fasciotomy</td>
<td>3</td>
<td>Yes</td>
</tr>
<tr>
<td>Fracture (sesamoid, splint)</td>
<td>6</td>
<td>Yes</td>
</tr>
<tr>
<td>Mass resection or excision</td>
<td>4</td>
<td>Yes</td>
</tr>
<tr>
<td>Neurectomy</td>
<td>7</td>
<td>Yes</td>
</tr>
<tr>
<td>Soft tissue wound débridement</td>
<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>Tenoscopy</td>
<td>5</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 2—Frequency of procedures performed (n = 101 total) during anesthetic maintenance and their classification as painful or not painful for the patients in Table 1.

Table 1—Summary of regression model variables factored by treatment drug and dose in a study of effects of postanesthetic sedation with romifidine or xylazine administered IV on quality of recovery from isoflurane anesthesia in horses.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Xylazine 100 ( \mu )g/kg</th>
<th>Xylazine 200 ( \mu )g/kg</th>
<th>Romifidine 10 ( \mu )g/kg</th>
<th>Romifidine 20 ( \mu )g/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>25</td>
<td>25</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>Signalment age (y)</td>
<td>7.2(2–15)</td>
<td>6.4(2–17)</td>
<td>7.2(2–17)</td>
<td>6.3(2–14)</td>
</tr>
<tr>
<td>Sex</td>
<td>Mare: 5, Stallion: 9, Gelding: 11</td>
<td>Mare: 3, Stallion: 5, Gelding: 17</td>
<td>Mare: 6, Stallion: 6, Gelding: 14</td>
<td>Mare: 6, Stallion: 10, Gelding: 9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>516 ± 87 (272–656)</td>
<td>528 ± 66 (525–490)</td>
<td>507 ± 77 (514–653)</td>
<td>498 ± 70 (494–665)</td>
</tr>
<tr>
<td>Breed</td>
<td>Arabian: 1, Quarter Horse: 4, Thoroughbred: 6, Other: 14</td>
<td>Arabian: 1, Quarter Horse: 1, Thoroughbred: 6, Other: 13</td>
<td>Arabian: 1, Quarter Horse: 4, Thoroughbred: 6, Other: 14</td>
<td>Arabian: 1, Quarter Horse: 4, Thoroughbred: 6, Other: 14</td>
</tr>
<tr>
<td>Total anesthesia time (min)</td>
<td>124 ± 45 (60–240)</td>
<td>117 ± 39 (65–205)</td>
<td>126 ± 44 (64–210)</td>
<td>132 ± 34 (75–200)</td>
</tr>
<tr>
<td>End-tidal isoflurane (%)</td>
<td>1.5 ± 0.2</td>
<td>1.5 ± 0.1</td>
<td>1.5 ± 0.1</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>Demand valve use</td>
<td>No: 13, Yes: 12</td>
<td>No: 18, Yes: 7</td>
<td>No: 16, Yes: 10</td>
<td>No: 13, Yes: 12</td>
</tr>
<tr>
<td>First movement time (min)</td>
<td>16 ± 7</td>
<td>17 ± 8</td>
<td>21 ± 9</td>
<td>26 ± 9</td>
</tr>
<tr>
<td>Total recovery time (min)</td>
<td>35 ± 16</td>
<td>40 ± 21</td>
<td>35 ± 15</td>
<td>50 ± 15</td>
</tr>
<tr>
<td>Painful procedure</td>
<td>No: 4, Yes: 21</td>
<td>No: 2, Yes: 23</td>
<td>No: 4, Yes: 22</td>
<td>No: 4, Yes: 23</td>
</tr>
<tr>
<td>VAS score (mm)</td>
<td>54 ± 27</td>
<td>65 ± 25</td>
<td>68 ± 22</td>
<td>69 ± 24</td>
</tr>
</tbody>
</table>

Data are number of animals or mean ± SD and median (minimum–maximum).
Visual analog scale scores among all horses ranged from 0 to 98, with a median score of 67 and a mean ± SD of 63 ± 25. Upon standing following a violent recovery, 1 Thoroughbred horse that had received 100 µg/kg of xylazine for recovery sustained a comminuted biarticular patern fracture and was euthanized. More minor injuries occurred in 13 other horses and were composed primarily of cuts or abrasions on the face. When present, injuries of any kind almost exclusively occurred in horses with a VAS ≤ 33. The VAS negatively correlated with subjective assessments of limb padding severity during recovery and with subjective assessments of ataxia once the horse was standing. Visual analog scale scores were also negatively correlated with several objective recovery events, namely the number of repetitive head slaps on the floor, the number of attempts to lie in sternal recumbency, and the number of attempts to stand.

Normalized Q-Q plots and Wilk-Shapiro tests indicated that patient age, the first movement time, and the total recovery time deviated significantly from a normal distribution. This was resolved by use of square root transformations of these variables, which were then subsequently used in regression modeling.

A backward and forward stepwise regression analysis identified the same 4 variables as significant predictors of VAS. Total anesthesia time measured in minutes had a slope of –0.19 ± 0.06 (mean ± SEM) and a P = 0.001. The Arabian breed, when compared with the reference of horses classified as other, had a slope of –20 ± 8 and a P = 0.01. Painful procedures (Table 2), when compared with nonpainful procedures as a reference, had a slope of –14 ± 7 and a P = 0.04. Administration of 20 µg of romifidine/kg, compared with the 100 µg/kg reference dose of xylazine, had a slope of 10 ± 5 and P = 0.05. The regression constant also significantly differed from zero, having a mean of 99 ± 8 and P < 0.001. The resulting regression equation predicting VAS was summarized as follows:

\[
\text{VAS} = 99 - (20 \times B_{\text{Arab}}) - (0.19 \times T_{\text{asw}}) - (14 \times P_{\text{pain}}) + (10 \times R_{20})
\]

where \(B_{\text{Arab}}\) indicates whether a horse is an Arabian breed (1 = true and 0 = false), \(T_{\text{asw}}\) is the total anesthesia maintenance time (in minutes), \(P_{\text{pain}}\) is the a priori assessment of a procedure as either painful (1 = true) or not painful (0 = false), and \(R_{20}\) indicates whether 20 µg/kg of romifidine was (1 = true) or was not (0 = false) used for postanesthetic sedation. No other variable considered in the model reached the criteria for inclusion at the stated level of significance (P ≤ 0.05). The coefficient of determination \(R^2\) for the model was 0.25.

In both backward and forward stepwise regression procedures, \(R_{20}\) was the last variable to be respectively retained or entered into the model. The mean VAS scores (in millimeters) for each postanesthetic treatment group were 65 ± 14 for 100 µg/kg of xylazine, 62 ± 14 for 200 µg/kg of xylazine, 63 ± 15 for 10 µg/kg of romifidine, and 61 ± 14 for 20 µg/kg of romifidine. Were the residual sum of squares not reduced by inclusion of other significant VAS predictors in the stepwise regression model, the postanesthetic drug treatment effect for \(R_{20}\) in the present study would not have been detectable. This is because other highly significant variable responses were not identically distributed across drug treatments and thereby behaved as confounding factors. For example, despite randomization, horses that received 20 µg/kg of romifidine also had the longest mean anesthetic times and underwent more procedures classified as painful (Table 2), compared with all other drug treatments groups. Although 20 µg/kg romifidine administration was associated with a 10-mm improvement on a 100-mm VAS via a multivariate analysis, longer and potentially painful procedures in this group would have obscured this treatment effect in a univariate analysis. Stepwise regression can control for confounding factors,20 which, in this study, enabled detection of a drug treatment effect for \(R_{20}\).

**Discussion**

In the present study evaluating healthy adult horses anesthetized with isoflurane for > 1 hour, the results supported the use of 20 µg/kg of romifidine for post-anesthetic sedation to improve recovery versus lower romifidine doses or xylazine. Four modifiers of recovery quality from isoflurane anesthesia were identified. Of these, only use of 20 µg/kg of romifidine was associated with an improvement in the VAS score. Painful procedures, longer anesthesia times, and Arabian horse breeds were all associated with poorer recovery quality. Of note, longer anesthetic duration and orthopedic surgeries for fractures, perhaps among the most painful equine noncolic surgical procedures, were also correlated with an increased risk of perioperative death in horses.2 It is not surprising that factors associated with violent anesthetic recoveries that increase risks of catastrophic injuries might likewise be associated with increased postanesthetic death.

The \(\alpha_2\)-adrenoreceptor agonists may improve recovery quality through at least 2 mechanisms. During recovery, isoflurane remains detectable in the end-tidal breath at concentrations approximately ≥ 10% of the inspired circuit concentration for at least 25 minutes.2 Subanesthetic inhalant concentrations by definition do not prevent voluntary movement, but nonetheless can exert important neurologic effects such as amnesia,11–13 diminished cognitive function,14,15 loss of proprioception,16–18 altered motor neuron function,19,20 and hyperalgesia.11,31 Sedatives administered during recovery delay attempts by the horse to stand.8–11 Thus, there is more time for inhaled anesthetic washout and return of neurologic functions, assuming alveolar ventilation is maintained, which should allow for a more sensible and coordinated recovery. The higher dose and longer duration of action of romifidine may have improved recovery simply because they provided the most time for isoflurane washout.

Another possible mechanism for improved VAS scores in the present study is the contribution of \(\alpha_2\)-adrenoreceptor agonists to analgesia. In horses, romifidine may produce more intense and longer-lasting antinociception to some nociceptive stimuli when compared with xylazine and detomidine,31 thereby preventing premature arousal and attempts to rise. Painful procedures (Table 2) were also a negative independent
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and mortality associated with poor anesthetic recovery could be important for decreasing the morbidity and ethical justifications, adequate postoperative analgesia, partial pressure equilibrium between arterial blood and the CNS, resulting in delayed anesthetic leaving low- and moderate-flow tissue reservoirs that would redistribute to the CNS, partial pressure equilibrium between vessel-rich groups such as brain, heart, and kidney occurs within minutes. However, equilibrium in tissues with lower flow, such as muscle and intestine, may take hours. At the other extreme, isoflurane fat is never achieved during most anesthetic periods. Consequently, as anesthetic time increases, total body anesthetic content also increases. During recovery, anesthetic leaving low- and moderate-flow tissue reservoirs can redistribute to the CNS, resulting in delayed alveolar washout and prolonged recovery time. If disparity, delayed alveolar washout should also prolong neurologic and behavioral effects associated with sub-anesthetic inhalant concentrations and thereby explain a negative association between anesthetic duration and recovery quality observed in the present study and a previous study.14

When controlled for other significant factors, Arabian horses tended to have a 20-mm lower VAS than other horse breeds in this study. In a survey of compulsive behaviors in stabled horses, Arabians exhibited a much higher incidence of stall walking and stall kicking than most other horse breeds26; it has been postulated that these activities may be related to anxiety or stress. Humans that are anxious, fearful, emotional, or impulsive preoperatively are more likely to exhibit delirium during anesthetic recovery.27 The effect of horse breed on recovery quality might more accurately reflect an effect of horse temperament.37

As with any clinical trial, this study had several limitations. First, the treatment codes were disclosed after VAS scoring by only a single evaluator; subjective recovery scores may have altered slightly if additional evaluators were included. However, the VAS tends to show relatively little intraobserver variability, even among less experienced individuals, and it correlates well with other composite scoring systems.38,39 Hence, additional evaluators probably would not have altered the significant findings. Second, there was no saline control against which to compare the different α₂-adrenoceptor agonist drugs and doses. This was a deliberate decision. There is sufficient evidence to indicate that recovery quality in healthy horses following 1 or more hours of inhalant anesthesia tends to be worse when no postanesthetic sedation is administered.9,10,40 Under these circumstances, use of a placebo control in patients that would likely increase the risk of poor recovery outcomes and patient morbidity would have been unethical and may not have met current standards of care for equine anesthetic practice. The 20 μg/kg IV romifidine dose increased VAS more than any other recovery drug treatment. This raises the question about whether this is the most effective dose of romifidine for equine recovery or whether even higher doses or different administration routes might yield additional benefit. On the other hand, horses recovering from anesthetics such as desflurane, which have a very low blood and tissue solubility, may not realize additional benefits from using longer-acting α₂-adrenoceptor agonists at high doses since the elimination rate for very insoluble inhaled agents is much more rapid.

The clinical trial reported here included only healthy horses anesthetized for 1 to 4 hours. Horses that are metabolically ill or exhausted might not need postanesthetic sedation since preexisting obtundation or weakness might already prolong recovery and allow sufficient time for anesthetic washout. Horses sedated for very brief periods with high doses of sedatives administered for premedication likewise may not need additional sedation for recovery. In these cases, sufficient postanesthetic sedation could be achieved by residual concentrations of premedication drugs.

Finally, the drug treatment, signalment, surgical, and anesthetic factors identified in the present study describe only 25% of the variability in VAS. We are left with the unsettling realization that 75% of patient variability in recovery quality remains unexplained. Future recognition of other determinants of recovery quality and development of preventative treatment for emergence delirium will be essential to reducing peri-anesthetic mortality risk in horses.

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