Sedative and Analgesic Effects of Romifidine in Horses

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ABSTRACT

The objective of this study was to confirm the sedative and analgesic effects of proposed doses of romifidine in horses. Twenty horses were enrolled in a prospective, randomized, complete, double-blind, crossover study. All horses received each of 2 dosages (40 and 120 µg/kg) of romifidine intravenously. Behavior criteria, quality of sedation, stance/posture, head ptosis, ear ptosis, lip separation, facial edema, degree of analgesia, and clinical assessment of analgesia were evaluated 30, 20, and 10 minutes before and 5, 15, 30, 45, 60, 75, 90, 105, 120, 150, and 180 minutes after romifidine administration. Heart rate, heart rhythm, respiratory rate, mucous membrane color, and rectal temperature were assessed at these same observation times. Romifidine produced dose-dependent effects in the degree and duration of sedation and analgesia. Rectal temperature, and respiratory and heart rates decreased, and second atrioventricular and sinus block were observed. One horse with evidence for heart disease developed ventricular tachycardia following the administration of 40 µg/kg IV romifidine. The administration of 40 and 120 µg/kg IV romifidine to horses produces dose-dependent sedation and analgesia. Horses that have pre-existing heart disease that are administered romifidine should be closely monitored.

INTRODUCTION

Alpha[2]-adrenoceptor agonists are used to produce sedation, analgesia, and muscle relaxation in horses. Romifidine (2-bromo-6-fluoro-2-imidazolidinhylidene-benzamine monohydrochloride) is a potent and selective alpha[2]-adrenoceptor agonist that produces pharmacologic effects typical for this group of drugs and characterized by sedation, muscle relaxation, reluctance to move, reduced responsiveness to environmental stimuli, bradycardia, decreased cardiac output, and reduced respiratory rate.[1–7] Relatively common arrhythmogenic effects include sinoatrial block, first and second atrioventricular (AV) block, bradycardia, and sinus arrhythmia.[3,4,8–13] Previous authors have ranked the efficacy of various alpha[2]-adrenoceptor agonists based upon these pharmacological effects from medetomidine, being the most efficacious, followed

by romifidine, detomidine, clonidine, and xylazine.[14–16] Romifidine produces the longest duration of sedative effects followed by detomidine, medetomidine, and xylazine.[4–7,17,18] The long duration of romifidine-induced sedation may be useful when control of patients is necessary for extended periods of time.[2,4,18]

To date, there have been no studies that have evaluated the pharmacologic and clinical effects of the lowest and highest doses (40 and 120 μg/kg IV) of romifidine recommended for clinical use in the same horses. The purpose of the present study was to determine and compare sedative, analgesic, select physiologic, and clinical effects of a low and high IV dose of romifidine in horses.

MATERIALS AND METHODS

Experimental Animals

Twenty adult horses (10 males and 10 females), 18 Thoroughbred and 2 Quarter horses, were used in this study. Age ranged from 3 to 18 years and weight ranged from 440 to 561 kg. Nineteen horses were judged to be in excellent physical condition based on physical examination, an electrocardiogram (ECG), hemogram, and blood chemical analysis. One horse had a IV/VI holosystolic murmur auscultated at the left base of the heart behind the left elbow. The murmur was presumed to be associated with mitral valve disease due to location, quality, and intensity. The horse was in excellent health otherwise and kept in the study. All horses were acclimated to a stockade. Food but not water was withheld the morning of each treatment day.

Study Design

The study was approved by the Animal Care and Use Committees of The Ohio State University and Louisiana State University The experiment was performed as a randomized, complete, double-blinded, crossover design. Each horse was treated with 2 doses of romifidine (Sedivet® 1%, Boehringer Ingelheim Vetmedica, Inc., Saint Joseph, MO, USA), 40 and 120 μg/kg IV romifidine,

over 2 periods separated by a minimum of 7 days. To avoid bias, administration of drug was performed by a person not involved in evaluating responses. No one involved in evaluating responses was present during drug administration. Each animal received 1 dosage during each treatment period.

The hair over both jugular veins was clipped 1 day prior to the start of study. An intravenous catheter (Abbocath®-T, 19GA × 5$^{1/2''}$, Abbott Laboratories, Chicago, IL, USA) was placed through a lidocaine (Butler lidocaine 2%, The Butler Company, Columbus, OH, USA) skin block into either the right or left jugular vein using aseptic technique. The catheter was filled with sterile heparinized saline to preserve potency. Horses were placed in a stock in a quiet room and allowed approximately 60 minutes to acclimate before making baseline observations. Data were collected at 30, 20, and 10 minutes before (baseline) and 5, 15, 30, 45, 60, 75, 90, 105, 120, 150, and 180 minutes after romifidine administration. All observations were made with the animals confined to a stock.

Behavior was categorized before and after the administration of 40 and 120 μg/kg IV romifidine: violent (out of control, lunges, rears, strikes, and/or kicks); very nervous (paces, paws, shifts weight, flicks ears, switches tail, raises and lowers head, and/or neighs intermittently); anxious (quiet but searching expression, flicks ears frequently); alert/calm (relaxed but responsive to external auditory, visual, and tactile stimuli); sedate/drowsy (response to auditory, visual, and/or tactile stimuli is decreased due to administered sedative, sleepiness, or illness); obtunded (recumbent, responds weakly to strong auditory, visual, and/or tactile stimuli); and comatose (recumbent, does not respond to strong auditory, visual, and/or tactile stimuli).

Four criteria were used to score the sedation: 0 = no sedation (normal frequency and velocity of movement, ear and neck carriage, eye alertness, lip apposition, postural tone, stance); 1 = mild sedation (slightly

decreased frequency and velocity of movement, lower ear and neck carriage, reduced eye alertness, appearance of lip separation, slight base-wide stance, slightly relaxed postural tone); 2 = moderate sedation (moderately decreased frequency and velocity of movement, obvious ear tip separation, lower, increased base-wide stance, appearance of crossed legs, buckled knees and/or fetlocks, more relaxed postural tone); and 3 = deep sedation (markedly decreased frequency and velocity of movement, pronounced ear tip separation, markedly lower neck carriage, greatly reduced eye alertness, extreme lip separation, markedly increased base-wide stance, increased occurrence and severity of crossed legs, buckled knees, and/or fetlocks, pronounced loss of postural tone). The duration of sedation was determined as the time from drug injection to return to a score of 1.

In addition, stance/posture (normal [0] or abnormal [1]), facial edema (absent [0] or present [1]), ear ptosis (centimeters between ear tips), lip separation (absent [0] or present [1]), and head ptosis were determined. Head ptosis was automatically assessed by a potentiometer integrated with a physiograph attached to the horse's head. Head drop was measured in volts that were then converted to centimeters distance from head to floor. The higher the head position, the greater the head-to-floor distance and the less the degree of head ptosis.

Analgesia was quantitatively assessed by hoof withdrawal reflex latency (HWRL), which was the time that elapsed (in seconds) from illumination of a heat lamp onto a prepared spot on the fetlock until limb withdrawal. Clinical assessment of response to the heat lamp was numerically scored as: 0 = no analgesia (normal aversion response to painful stimulus); 1–2 (delayed aversion); 3–4 (aversion response time is moderately increased and the magnitude of response is moderately reduced); and 5–6 = profound analgesia, (aversion response time is dramatically prolonged). The duration (minutes) of analgesia from the time of drug administration was determined.

Heart rate and rhythm were determined by auscultation over 1 minute intervals, and arrhythmias were further characterized by ECG during the same recording interval. Respiratory rate was determined by auscultation and chest wall excursion. Mucous membrane color (pale, pink, red, purple, dark blue, and pale blue) and the rectal temperature were determined.

Data Analysis

Data was divided into 4 main categories: continuous (HWRL, head ptosis, ear ptosis, heart and respiratory rates, rectal temperature), dichotomous (facial edema, lip separation, heart rhythm, stance), ordinal (sedation, analgesia scored), and nominal variables (behavioral attitude, mucous membrane color). Descriptive statistics (mean and SD) were calculated for all measured parameters. The baseline values for each continuous response were calculated as the mean before romifidine administration (−30, −20, −10) and were investigated as possible covariates. The initial model tested was a repeated measures analysis of covariance (ANCOVA). If the covariate was eliminated, then a repeated measures analysis of variance (ANOVA) was conducted. All dichotomous, ordinal, and nominal data were subjected to appropriate contingency tables (McNemar's test, exact test for marginal homogeneity, and Bowker's test of symmetry, respectively). Statistical significance was considered at $P < 0.05$.

RESULTS

No significant differences were observed between pretreatment times for any of the evaluated variables for the 2 treatment groups (40 and 120 μg/kg IV romifidine). Romifidine appeared to modify behavior in a dose- and time-dependent manner. The administration of 40 μg/kg IV romifidine produced sedate/drowsy appearance in all horses for at least 45 minutes. This appearance began to abate at 60 minutes after drug administration when most horses were alert yet calm. One horse still appeared sedate at
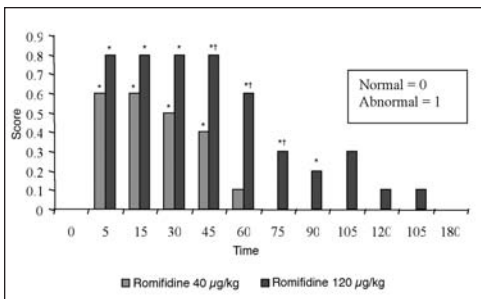
Figure 1. Stance and posture following romifidine administration in horses.

*Significant difference from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$ (40 μg/kg IV romifidine < 120 μg/kg IV romifidine).
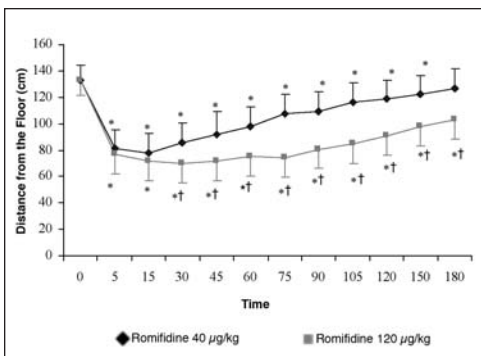

Figure 2. Head ptosis following romifidine administration in horses.

*Significantly different from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$ (40 μg/kg IV romifidine < 120 μg/kg IV romifidine).

180 minutes. The 120 μg/kg IV dose of romifidine produced rapid sedation in all horses that persisted for at least 60 minutes. Eleven of 20 horses were still sedate at the 180 minute observation period. More horses were significantly more sedate after the administration of 120 μg/kg IV compared with 40 μg/kg IV romifidine at 90, 105, 120, and 180 minutes. No violent behavior was seen in any horse at any time. Romifidine increased the categorical assessment of sedation scores in all horses (Table 1). Horses administered 120 μg/kg IV romifidine exhibited consistently greater scores (deeper sedation) than horses administered 40 μg/kg IV romifidine (Table 2). Both the degree and duration of sedation were dose dependent.

An abnormal stance was observed in 12 horses 15 minutes after the administration of 40 μg/kg IV romifidine. The number of horses with an abnormal stance decreased thereafter; however, a significant difference compared with baseline was still observed for 45 minutes and all horses had a normal stance after 75 minutes. Sixteen of 20 horses had an abnormal stance 5 minutes after the administration of 120 μg/kg IV romifidine. Only 1 horse had an abnormal stance at 120 minutes, and none were abnormal at 180 minutes. More horses demonstrated an abnormal stance that was considered significantly different at 45, 60, and 75 minutes after the administration of 120 μg/kg IV romifidine (Figure 1). The most common stance observed after either dose of romifidine was a base-wide stance of front, rear, or all 4 legs.

Both doses of romifidine produced head ptosis (Figure 2). Head ptosis lasted for 150 and 180 minutes for 40 and 120 μg/kg IV romifidine, respectively. Maximum head ptosis was observed at 15 minutes for 40 μg/kg and at 30 minutes for 120 μg/kg. Horses administered 120 μg/kg IV romifidine demonstrated significantly greater head ptosis than horses administered 40 μg/kg IV romifidine at 30 to 180 minutes.

Lip separation was observed in all 20 horses at 15 and 30 minutes after 40 μg/kg IV romifidine. Nine of 20 horses still had lip separation at 75 minutes after romifidine administration. All horses had lip separation at 5 minutes after 120 μg/kg IV romifidine. This effect persisted for 75 minutes and was different between the 2 treatment dosages from 60 to 150 minutes.

Facial edema was absent in all horses before romifidine administration. Facial edema was present in 16 of 20 horses at 5 minutes after 40 μg/kg IV romifidine and decreased from 45 to 105 minutes. Only 1 horse had facial edema from 120 to 180 minutes. Seventeen of 20 horses had facial edema at 5 minutes after 120 μg/kg IV romifidine. All 20 horses in this group showed facial edema at 15 minutes, and 3

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Table 1. Assessment of Quality of Sedation (AQS) Following Romifidine Administration in Horses.

Treatment	Time	0 none	1 mild	2 mod	3 deep	Treatment	Time	0 none	1 mild	2 mod	3 deep
baseline	20					baseline	20				
	5*†		2	16	1		5*			6	14
	15*†		1	17	2		15*			2	18
	30*†		2	17	1		30*			6	14
	45*†		12	7	1		45*			11	9
40 µg/kg	60*†		16	4		120 µg/kg	60*		1	13	6
IV	75*†	2	17	1		IV	75*		5	11	4
romifidine	90*†	6	13	1		romifidine	90*		8	11	1
	105*†	11	8	1			105*	1	8	10	1
	120*†	13	7				120*	1	11	8	
	150*†	16	4				150*	4	12	4	
	180†	18	2				180*	6	12	2	

Numbers within grids are frequency of observation.
*Significantly different from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$ (40 µg/kg IV romifidine < 120 µg/kg IV romifidine).

horses still had facial edema at 180 minutes. The difference in facial edema between the 40 and 120 µg/kg IV romifidine doses was significant at 45, 60, 75, 90, 105, and 120 minutes.

Both doses of romifidine produced separation of the ear tips at 5 minutes after the administration of romifidine (Figure 3). Horses administered 120 µg/kg IV romifidine demonstrated a significant increase from baseline at all observation points. The distance between the ear tips was greatest at 105 minutes. The degree of ear ptosis was significantly greater at 75, 105, 120, and 180 minutes when 120 µg/kg IV romifidine was compared with romifidine 40 µg/kg.

The magnitude and duration of analgesia was significantly greater after the administration of 120 µg/kg IV romifidine (Table 2; Figures 4 and 5).

Decreases in respiratory rate and sinus bradycardia, second AV block, or sinus block (<5 seconds) were common after the administration of either dose of romifidine (Table 3; Figure 6). One horse exhibited a transient period of ventricular tachycardia at the 75-minute recording period after being administered 40 µg/kg IV romifidine.

Mucous membrane color was pink in all horses prior to romifidine administration.

Both the 40 and 120 µg/kg IV doses of romifidine produced purple mucous membranes that were significantly more obvious when horses were administered 120 µg/kg compared with those that received 40 µg/kg IV romifidine at 30, 45, 60, 75, 90, and 105 minutes.

Rectal temperatures were significantly decreased from baseline to 60, 75, 90, 105, 120, and 180 minutes after administration of 40 µg/kg IV romifidine and at 90, 105, 120, 150, and 180 minutes after 120 µg/kg IV romifidine. There was a significant difference between doses at 45 and 60 minutes (Table 3).

DISCUSSION

Our experiments confirm and extend previous reports evaluating the sedative and analgesic effects of romifidine in horses. The intravenous administration of romifidine produced dose-dependent changes in categorical and objective measures of behavior, and response to noxious stimuli and physiologic variables. These changes were similar to those previously reported for other alpha$_2$-adrenoceptor agonists; lower doses (80 µg/kg IV) of romifidine suggesting that romifidine is a safe and effective sedative and analgesic in adult horses.[4,5,8,18]
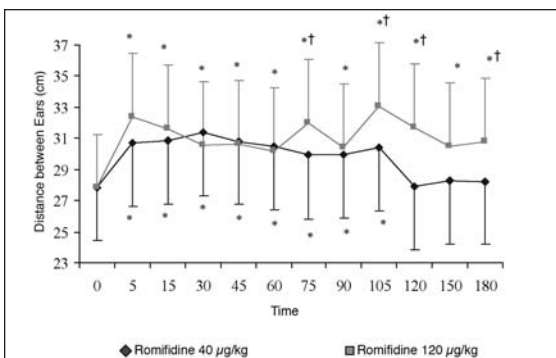
Figure 3. Ear ptosis following romifidine administration in horses.

*Significantly different from baseline, $P < 0.05$.

†Significant difference between treatments, $P < 0.05$ (40 µg/kg IV romifidine > 120 µg/kg IV romifidine).

Table 2. Estimated Duration of Effect of Sedation (Assessment of Quality of Sedation (AQS)) and Analgesia (Hoof Withdrawal Reflex Latency (HWRL)) Based on a Mean Score Over 1 (mild sedation or analgesia) of AQS and HWRL Following Romifidine Administration in Horses.

Effect/Dose	Estimated Duration of Effect (minutes)
Sedation (AQS)	
40 µg/kg IV romifidine	75
120 µg/kg IV romifidine	180
Analgesia (HWRL)	
40 µg/kg IV romifidine	105
120 µg/kg IV romifidine	180

Various studies have evaluated the sedative, analgesic, and anesthetic sparring effects of alpha$_2$-adrenoceptor agonists in horses.[4,5,8,10,12,13,16–19] The majority of these studies were designed to compare the sedative, analgesic potency, and duration of effects of romifidine to other alpha$_2$-adrenoceptor agonists (xylazine, detomidine) and to quantify changes in cardiorespiratory variables. Collectively, these studies indicate that romifidine and other alpha$_2$-adrenoceptor agonists are capable of producing significant, dose-dependent sedation, increases in the horses' tolerance to a painful stimulus, and depression of cardiorespiratory function. Alpha$_2$-adrenoceptor agonists produce excellent muscle relaxation of the muscles of the head, neck, and ears followed by drooping of the head, ears, and lips.[4,5,18,20] These effects are centrally mediated, are well correlated with degree of sedation, and have become widely accepted as objective methods for the assessment of the depth and duration of the sedation provided by alpha$_2$-adrenoreceptor agonists.[4,5,10,18,20–23] We observed a pronounced difference in these variables when doses of 40 and 120 µg/kg IV romifidine were adminis-

Table 3. Mean and SD of Respiratory Rate and Rectal Temperature Following Romifidine Administration in Horses.

| Time (minutes) | Respiratory Rate (bpm) | | Rectal Temperature (˚C) | |
	40 µg/kg IV romifidine	120 µg/kg IV romifidine	40 µg/kg IV romifidine	120 µg/kg IV romifidine
baseline	12 ± 2	12 ± 2	37.6 ± 0.6	37.6 ± 0.6
5	9 ± 3*†	12 ± 3	37.3 ± 0.57	37.6 ± 0.57
15	9 ± 3*	11± 3	37.6 ± 0.57	37.6 ± 0.57
30	8 ± 3*	10 ± 3*	37.6 ± 0.57	37.7 ± 0.57
45	7 ± 3*	9 ± 3*	37.5 ± 0.56†	37.7 ± 0.57
60	7 ± 3*	8 ± 3*	37.3 ± 0.56*†	37.6 ± 0.57
75	8 ± 3*	7 ± 3*	37.3 ± 0.58*	37.5 ± 0.57
90	8 ± 3*	7 ± 3*	37.2 ± 0.57*	37.4 ± 0.57*
105	8 ± 3*	7 ± 3*	37.3 ± 0.57*	37.2 ± 0.57*
120	7 ± 3*	7 ± 3*	37.2 ± 0.58*	37.2 ± 0.57*
150	7 ± 3*	7 ± 3*	37.1 ± 0.58*	37.2 ± 0.57*
180	8 ± 3*	7 ± 3*	37.1 ± 0.58*	37.1 ± 0.57*

*Significantly different from baseline, $P < 0.05$.

†Significant difference between treatments, $P < 0.05$ (40 µg/kg IV romifidine < 120 µg/kg IV romifidine).
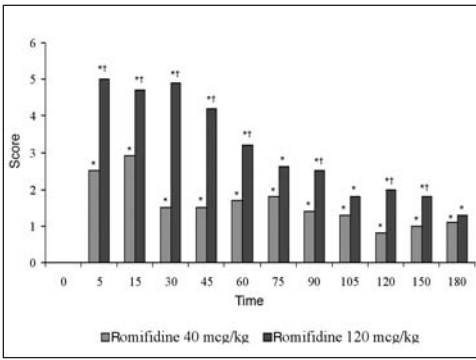
Figure 4. Analgesia assessment scores for HWRL following romifidine administration in horses.

*Significant difference from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$ (40 µg/kg IV romifidine < 120 µg/kg IV romifidine).
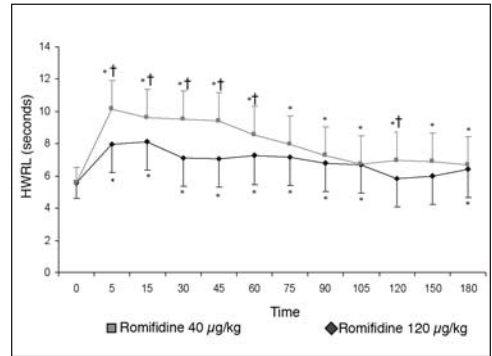

Figure 5. HWRL following administration of romifidine in horses.

*Significantly different from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$ (40 µg/kg IV romifidine < 120 µg/kg IV romifidine).
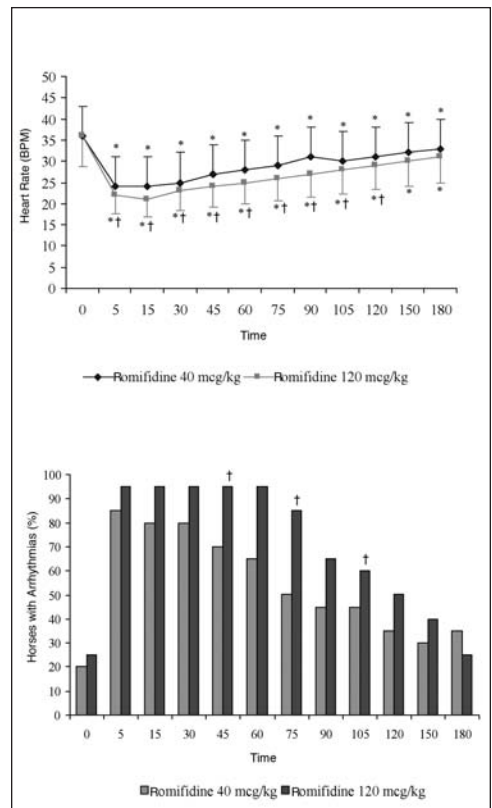

Figure 6. Heart rate and incidence of arrhythmias following romifidine administration.

*Significantly different from baseline, $P < 0.05$.
†Significant difference between treatments, $P < 0.05$.

tered. The administration of 40 and 120 µg/kg IV romifidine in our study produced qualitatively similar changes to those previously reported for xylazine, detomidine, and medetomidine.[4,5,8,10,17] Sedation was apparent within 5 minutes of IV drug administration and maximal effect persisted for 45 and 60 minutes for all horses. The sedative effects gradually decreased thereafter although more than half of the horses administered 120 µg/kg IV romifidine remained sedated for longer than the 3-hour data collection period. Our findings describing the sedative qualities of romifidine are similar to those reported for xylazine and detomidine but vary quantitatively with regard to the duration of drug-related effects.[5,8,10,18] Previous studies have suggested that 120 µg/kg IV romifidine produces sedation that lasted for less than 90 minutes.[5,18,20] We used both objective and strict categorical measures of sedation and determined a longer duration (>180 minutes) of sedation for the same dose. One group of investigators suggested a ceiling effect for maximum sedation followed the administration of 80 µg/kg IV romifidine and that larger dosages reduced its sedative qualities resulting in a shorter duration of effect.[5] Our study and those of others do not support this observation since we did not observe a reversal of sedative effects when 120 µg/kg IV romifidine was administered.[4,18,20] We did not determine the

sedative characteristics of intermediate doses of romifidine and therefore cannot comment on a ceiling effect following the administration of 80 µg/kg IV romifidine although others have not observed this type of response.[4,18,20] Collectively, these data suggest that romifidine produces dose-dependent sedation and that the methods (degree or duration of head ptosis, ataxia, response to auditory or physical stimuli) and number of descriptors used to evaluate sedation are likely responsible for the reported differences in drug effect and duration.

Previous studies in horses have suggested that romifidine produces less instability and ataxia compared with other commonly used alpha$_2$-adrenoreceptor agonists.[2,5,12] However, when romifidine was administered at 120 µg/kg and horses were forced to walk over a wooden bar, some horses fell over.[18] We did not evaluate ataxia in horses administered romifidine and forced to walk, but the administration of both the low and high doses of romifidine produced a characteristic base-wide posture of both front and rear legs in horses. None of the horses in the study showed unacceptable instability or fell during the experiment. It is likely that any differences reported between alpha$_2$-adrenoceptor agonists regarding ataxia are dose dependent.

Analgesia is an important quality of alpha$_2$-adrenoceptor agonists.[12] It is interesting, therefore, and somewhat surprising that the analgesic effects of romifidine have not been emphasized until recently.[16] Early reports suggested that romifidine was devoid of analgesic activity and that its only benefits (other than sedation) were less ataxia and longer duration of sedative action compared with detomidine and xylazine.[5] Analgesia was evaluated by applying a constant electrical current to the withers, coronary band, and perineal area; results demonstrated romifidine did not produce analgesic effects.[5] These early studies have been questioned based on more recent studies demonstrating that 80 µg/kg IV romifidine produces analgesia that attains maximum effect within 15 minutes and persists for up to 60 minutes when a controlled

electrical stimulus was applied to the coronary band.[16] We used a standardized thermal noxious stimulus similar to that reported by others.[24,25] The hoof withdrawal reflex was capable of producing a readily identifiable pain-threshold response that was qualitatively similar among subjects and did not cause significant tissue damage. We demonstrated that romifidine produced a significant increase of the latency time to hoof withdrawal in horses administered both 40 and 120 µg/kg IV romifidine and that this effect was significantly greater following the administration of 120 µg/kg IV romifidine, suggesting that romifidine produces dose-dependent analgesia. In our study, the duration of analgesia produced by 40 µg/kg IV romifidine was comparable to that reported for 20 µg/kg IV detomidine in a electrical current model[5] and 1.1 mg/kg IV xylazine in a dental dolorimetry model,[26] and that the duration of analgesia produced by 120 µg/kg IV romifidine was comparable to 160 µg/kg IV detomidine in an electrical current model.[10]

Facial edema, which can be caused by venous congestion that occurs when horses hold their head down after sedation, increased significantly following administration of romifidine in both the doses we studied. Previous studies had demonstrated that its severity is correlated with the duration and degree of lowering of the head.[18,20] Nasal edema often accompanies facial edema and may lead to respiratory compromise.[17,20] In our study, facial edema occurred more frequently in horses administered 120 µg/kg IV romifidine. Respiratory noise was observed in horses administered low- and high-dose romifidine in our studies, although none of the horses appeared compromised, and none of them needed support of the head to breathe properly. Evaluation of the color of the mucous membranes is often used to subjectively evaluate tissue perfusion, but may be inaccurate in sedated horses due to the development of venous congestion when horses have their heads lowered. The mucous membranes generally become injected when horses lower their head. Similar to facial

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edema, the incidence of injected mucous membranes was greater in horses administered 120 μg/kg IV romifidine.

Alpha[2]-adrenoceptor agonists decrease respiratory rate and heart rate. Hypoventilation usually does not occur because the depth of breathing increases to maintain minute ventilation.[3,6–9,13,18] Others have reported that larger doses of romifidine caused less of a decrease in respiratory rate than lower doses.[7,18,20] We observed a significant decrease in respiratory rate following both doses of romifidine but are unable to comment on gas exchange because arterial blood gas analysis was not performed.

Alpha[2]-adrenoceptor agonists induce a vagally mediated reflex bradycardia, secondary to increases in arterial blood pressure and partly from direct central sympathetic depression.[3,8,10,12] Previous studies in horses suggest that IV romifidine (40, 80, and 120 μg/kg) decreases heart rate similar to reductions produced by xylazine, detomidine, and medetomidine.[3,8,9,13,17] We noted significant decreases in heart rate that lasted throughout the observation period (180 minutes) after administration of 40 and 120 μg/kg IV romifidine, a duration that was longer than previously reported.[2,7] In addition, horses that received 120 μg/kg IV romifidine had a significantly lower mean heart rate for longer durations than horses that received 40 μg/kg IV romifidine. Others have demonstrated a similar response and moderate decreases in heart rate when higher doses (80 and 120 μg/kg) of romifidine are administered,[2,4,18] suggesting that heart rate decreases in a dose-dependent manner.

Second AV block may be detected in normal awake horses and is believed to be a physiologic variant in horses at rest.[4,8,27] Twenty to 25% of the horses we evaluated had second AV block prior to romifidine administration. Sinus and AV block induced by alpha[2]-adrenoceptor agonists are often associated with bradycardia and attributed to decreased sympathetic outflow from the central nervous system and increased vagal tone.[3,4,8,10-13] Second AV block occurred following the administration of both doses of romifidine but was more common and persistent when 120 μg/kg IV romifidine was administered. The incidence of arrhythmias declined as heart rate increased and signs of sedation decreased. Ventricular tachycardia is an uncommon event and has not been reported in the literature after administration of alpha[2]-adrenoceptor agonists in healthy horses. The development of ventricular tachycardia in 1 of the horses at 75 minutes after receiving 40 μg/kg IV romifidine was not expected. Ventricular tachycardia occurred in an older horse with a preexisting IV/VI systolic cardiac murmur with no related clinical signs. The administration of 120 μg/kg IV romifidine to the same horse did not result in a ventricular tachycardia, suggesting that its development may have been serendipitous although a drug-related relationship cannot be discounted.

Romifidine produced dose-dependent sedation and analgesia and similar cardiorespiratory effects including second AV block to those reported for other alpha[2]-adrenoceptor agonists. The development of ventricular tachycardia in 1 horse with a cardiac murmur suggests that the administration of alpha[2]-adrenoceptor agonists to horses with cardiovascular disease should be carefully monitored.

ACKNOWLEDGMENTS

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