Practical Standing Chemical Restraint of the Horse

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Knowledge of the pharmacology of sedatives, tranquilizers, and analgesics allows equine veterinarians to provide safe restraint for standing procedures. Author's address: Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, 1900 Coffey Road, Columbus, Ohio 43210; e-mail: John.Hubbell@cvm.osu.edu. © 2009 AAEP.

1. Introduction

Many surgical and medical procedures can be accomplished in the standing horse if appropriate combinations of physical and chemical restraint are employed. The ability to perform procedures in the standing position is more important in the horse than in other species because of the greater risk of complications associated with anesthesia in the horse.[1] The goal of most standing restraint is to produce a quiet, calm horse that is immobile and does not react to stimuli or manipulation. Analgesia should be provided if the intended procedure is expected to be painful.

There are nine drugs approved for use in horses for standing chemical restraint: acepromazine, butorphanol, chloropent, detomidine, pentazocine, promazine, romifidine, triflupromazine, and xylazine. Of these, only five drugs (acepromazine, butorphanol, detomidine, romifidine, and xylazine) are commercially marketed by pharmaceutical houses. Other drugs, such as morphine and fentanyl, are used with some frequency for standing chemical restraint but are not labeled for use in the horse. No single drug produces "ideal" standing chemical restraint in every horse. Although the majority of sedative and analgesic drugs used for restraint are labeled for use as "sole" agents, the majority of equine veterinarians use them in combination with the goal of optimizing the onset, quality, and duration of the alteration in mental state while minimizing potentially deleterious side effects. Many combinations are recommended in the literature, but relatively few have been rigorously studied scientifically. The potential number of combinations for the nine approved drugs (511 combinations) and the five commercially marked drugs (31 combinations) suggests that it is unlikely that such studies will be completed.

2. Phenothiazine Tranquilizers

Phenothiazine tranquilizers are used to produce calming.[2] Phenothiazine tranquilizers are not believed to produce analgesia, but they do enhance the analgesic activity of other drugs such as α-2 agonists and opioids. Phenothiazines activate when given orally, intramuscularly, and intravenously by blocking the action of neurotransmitters (dopamine) centrally and peripherally and causing α adrenergic blockade that can lead to arterial hypotension.[3] This is of particular concern in excitable horses, horses that have hemorrhaged, or dehydrated

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horses. Phenothiazines do not significantly affect respiration, but respiratory rate frequently decreases. In stallions and geldings, phenothiazine administration rarely causes persistent penile paralysis (priapism). Benztropine mesylate[a] (8 mg, IV, total dose to two adult horses) has been used to treat priapism with resolution of effect within 10 min.[4] Others report the injection of 10 mg of 1% phenylephrine[b] directly into the corpus cavernosum penis.[5] In both reports, early intervention is the key to success. Horses not responding to pharmacologic treatment may require surgical irrigation of the corpus cavernosum penis.

Acepromazine[c] is supplied as a 1% solution (10 mg/ml) for injection. Onset of action occurs within 15–30 min, but peak effects may not be seen for up to 45 min, a factor that may limit its use as a sole agent in clinical practice. The duration of sedation depends on the dose but may last for 6–10 h (Table 1). Acepromazine cannot be relied on to make an aggressive horse a malleable patient. Increasing the dose does not usually produce a greater effect but may increase the duration of effect. Minimal muscle relaxation or ataxia occurs, and therefore, acepromazine can be used to reduce awareness as an aide to breaking and training or to transporting the horse. The best index of the degree of sedation with acepromazine is the presence of protrusion of the penis in male horses. In addition, the eyelids will droop, and the third eyelid will protrude. Phenothiazine tranquilizers interfere with platelet function, and thus, their use should be avoided if this is a concern.[6] Hypovolemic horses administered acepromazine may become acutely hypotensive with fainting and may become recumbent. Treatment of hypotension should include large volumes of IV flu-

Table 1. Dose of Drugs Frequently Used for Standing Chemical Restraint

Drug	Dose and Route	Onset of Effect and Duration	Comments
Acepromazine	0.02–0.05 mg/kg, IM, IV	20–40 min, IV, IM Duration: 4–6 h	Use cautiously in stressed or hypotensive horses Potential for priapism in males
Xylazine	0.2–1.0 mg/kg, IV	3–5 min, IV	Ataxia produced, head down posture
	1.0–2.2 mg/kg, IM	10–20 min, IM Duration: 20–30 min, IV	Start with low dose and repeat as needed
Detomidine	0.01–0.02 mg/kg, IV	3–5 min, IV	Ataxia produced, head down posture
	0.02–0.04 mg/kg, IM	10–20 min, IM	Start with low dose, repeat as needed
	0.06 mg/kg, PO	30–45 min, PO Duration: 45–60 min, IV	
	Infusion (IV) 10 μg/kg bolus followed by 0.5 μg/kg/min for 15 min, then 0.3 μg/kg/min for 15 min, then 0.1 μg/kg/min.[30]	Decrease infused dose when procedures are prolonged	Dosing at constant rates prolong effects
Romifidine	0.04–0.120 mg/kg, IV	2–5 min, IV Duration: 2–3 h, IV	Less head down posture Reduced ataxia, reduced analgesia
Butorphanol	0.01–0.03 mg/kg, IV	3–5 min Duration: 1–2 h, IV	Usually used in combination with a sedative or tranquilizer. Some twitching.
	Infusion: 10–15 μg/kg/min[32]		Improves wellbeing after colic surgery
Buprenorphine	0.006 mg/kg, IV	Duration: 10–20 min	Longer acting opioid. Use in conjunction with xylazine or detomidine
Morphine	0.3–0.5 mg/kg, IV	3–5 min Duration: 2–6 hr, IV	Sedate with xylazine or detomidine prior to administering morphine. Potential for excitement. Reversible with naloxone.

ids. Acepromazine should be avoided if testing for allergens, because the drug has antihistaminic properties. No specific antagonist for phenothiazine tranquilizers is known. Acepromazine is available in an oral gel form in the United Kingdom.

3. α-2 Agonists

α-2 agonists produce sedation with muscle relaxation, ataxia, and analgesia when given orally, intravenously, or intramuscularly. Xylazine, detomidine, and romifidine are approved for use in the horse in the United States. Medetomidine and dexmedetomidine are used in other countries but are not currently approved for use in the United States. The α-2 agonists produce a number of cardiorespiratory and other side effects, the significance of which are dose dependent in the clinical dose range. Heart rate decreases, and sinus arrhythmia, first degree atrioventricular blockade, and second degree atrioventricular blockade are common. Arterial blood pressure is initially increased because of drug-induced increases in peripheral vascular resistance.[7] Hypertension may be sustained (20–60 min), particularly when detomidine and romifidine are used.[7,8] Decreases in heart rate and increases in peripheral vascular resistance produce significant decreases in cardiac output, often to levels 50% of the pre-drug values. Respiratory rate is usually decreased, but tidal volume increases to compensate for the drop.[9] Relaxation of the muscles of the upper airway occurs and can predispose the horse to stridor.[9] The administration of an α-2 agonist decreases salivation, gastric secretions, and gastrointestinal motility, and it also increases urine volume.[10,11] Swallowing is depressed, and thus, passage of nasogastric tubes may be more difficult. Other incidental effects of α-2 administration include increases in intrauterine pressure, hyperglycemia, and hypoinsulinemia.[12,13]

The level of sedation produced by administration of an α-2 agonist is more pronounced than that produced by phenothiazine administration. Depending on the dose and drug administered, horses assume a "head-down" or "saw horse" stance and frequently shift their weight from side to side. Xylazine[d] is useful for restraint for procedures on the head, neck, and forequarters, but some researchers have expressed concern about its suitability when used as the sole agent for procedures on the hindquarters because of the potential for rapid arousal (startling) and kicking.[14] This view is supported by appearance of profound sedation typified by the extreme head-down posture associated with large doses of xylazine or detomidine. Unprovoked aggression has been reported after the administration of xylazine or detomidine.[15] Combining α-2 agonists with other agents often permits the use of reduced doses, which lessens the head-down posture and causes the horse to stand more squarely on all four feet.[3,16,17] Detomidine[e] is a more specific α-2 receptor agonist than xylazine, and it has an α-2/α-1

specificity of 260:1 compared with 160:1 for xylazine (data from rat studies).[18] Detomidine is ~100 times more potent than xylazine and has a duration of action approximately twice as long. Detomidine is used alone and in combination with opioids (butorphanol and nalbuphine) to produce standing chemical restraint for a wide variety of procedures.[19–21]

Romifidine[f] is an α-2 adrenoreceptor agonist with an α-2/α-1 selectivity ratio of 340:1, which places its selectivity intermediate among the currently available α-2 agonists. Romifidine causes dose-related sedation when administered intravenously or intramuscularly, and it has a rapid onset of action and a duration of action similar to detomidine.[18,22] The depth of maximal sedation with romifidine is reported to be less than that seen with detomidine as judged by the lowering of the head. Romifidine-induced ataxia is also less severe than that of other α-2s.[23] The analgesic effects of romifidine are somewhat controversial.[22,24] Clearly, the analgesia that is produced is of shorter duration than the sedative effects. Medetomidine[g] is the most specific of the available α-2 agonists, and it has an α-2/α-1 selectivity ratio of 1620:1. Doses of medetomidine in the range of 5–7 μg/kg body weight cause deep sedation with significant ataxia.[25,26] Analgesia is greater than or equal to that seen after detomidine, and the duration of action is somewhat shorter than that seen with detomidine.

α-2 agonists can be administered intravenously, intramuscularly, or orally.[27,28] IM drug administration is easily accomplished, but the onset of drug action is slower than after IV administration (<5 min for IV compared with 10–15 min for IM). The intensity of the cardiorespiratory side effects after IM injection is reduced, presumably because of the lower plasma concentration of unbound drug. IV administration produces a quicker onset of action and an increased intensity of effect but a shorter duration of effect. Currently, oral administration is saved for occasions when the horse is not amenable to injections because of inconsistent effects. Oral (sublingual) administration of detomidine (0.06 mg/kg body weight) has been shown to produce profound sedation 45 min after administration.[27]

Infusions of α-2 agonists, including detomidine and medetomidine, for standing surgery and as adjuncts to IV anesthesia are gaining popularity.[29,30] The use of constant rate infusion reduces the ups and downs of repeat bolus administration and frequently lowers the total dose of drug administered.

4. Opioids

Opioids are used to produce analgesia and augment the effects of sedatives and tranquilizers, but when they are administered alone to pain-free animals, they can cause nervousness and excitability. Butorphanol[h] is a synthetic opioid agonist/antagonist that is approved for use in the horse for the treatment of abdominal pain.[30,31] Butorphanol is less prone to cause excitement than morphine or fenta-

nyl, but ataxia can be severe at high doses. Butorphanol is frequently combined with α-2 agonists.[16,17,21] When combined with xylazine, reduced doses of xylazine are usually used; this results in a horse that is less ataxic than with full doses of xylazine, but jerks and twitches may occur and the horse may head press. The analgesia produced is insufficient to blunt the pain of procedures involving incisions, and therefore, local anesthetic blocks should be incorporated. Butorphanol is also used in combination with detomidine and romifidine. It has been suggested that the inclusion of butorphanol reduces the incidence of unexpected arousal. Buprenorphine[i] has been used in a similar manner to butorphanol.[19,20]

Other opioids including morphine[j] and pentazocine[k] have also been used to produce standing chemical restraint.[32,33] The combination of xylazine and morphine produces a profoundly obtunded animal.[34] Xylazine administration should precede morphine to prevent opioid-induced excitement. The head should be elevated and a nose twitched placed, if necessary, because the horse will tend to lean forward. Horses remain sensitive to touch, and therefore, local anesthesia should be incorporated with the technique. Naloxone[l] can be used to antagonize morphine. Renarcotization (excitement) occasionally occurs and is best treated by repeat administration of naloxone or tranquilizer administration.

5. Acepromazine and α-2 Agonist Combinations

The combination of acepromazine with an α-2 agonist allows for a reduction in the dose of both agents, which reduces the cardiopulmonary side effects and ataxia.[3] Typically, 0.02–0.03 mg/kg of acepromazine is combined with 0.2–0.5 mg/kg of xylazine. The drugs can be combined in the same syringe and are usually given IV.

6. Ketamine Infusion

Ketamine[m] infusions are beginning to be incorporated into protocols for analgesia.[35–37] The dose administered ranges from 0.4 to 0.8 mg/kg/h and is given at a constant rate. The effectiveness of the technique seems to depend on the type of pain being induced or treated, and excellent results have been seen for patients with burns. Further research is needed to determine if this technique should be added to the armamentarium of the equine practitioner.

7. Lidocaine Infusion

Lidocaine infusions are used as adjuncts to inhalant anesthetics and for post-operative pain. The administration of lidocaine[n] could have additional benefits as part of standing chemical restraint, but there are concerns about the degree of ataxia produced. The intra-operative administration of lidocaine (50 μg/kg/min) reduces the required dose of inhalant.[38] In conscious horses, lidocaine reduces the response to a heat stimulus, but visceral pain is not affected.[39] Lidocaine requires a constant rate infusion to be effective systemically. Infusions are usually well tolerated, but bolus administration can be associated with hypotension.

References and Footnotes

1. Johnston GM, Eastment JK, Wood JLN, et al. The confidential enquiry into perioperative equine fatalities (CEPEF): mortality results of Phases 1 and 2. *Vet Anaesth Analg* 2002;29:159–170.
2. Muir WW. Anxiolytics, nonopioid sedative-analgesics, and opioid analgesics. In: Muir WW, Hubbell JAE, eds. *Equine anesthesia: monitoring and emergency therapy*, 2nd ed. St. Louis, MO: Saunders Elsevier, 2009;186–190.
3. Muir WW, Skarda RT, Sheehan WC. Hemodynamic and respiratory effects of a xylazine-acetylpromazine drug combination in horses. *Am J Vet Res* 1979;40:1518–1522.
4. Wilson DV, Nickels FA, Williams MA. Pharmacologic treatment of priapism in two horses. *J Am Vet Med Assoc* 1991;199:1193–1184.
5. Pauwels F, Schumacher J, Varner D. Priapism in horses. *Compend Cont Educ Pract Vet* 2005;27:311–315.
6. Barr SC, Ludders JW, Looney Al, et al. Platelet aggregation in dogs after sedation with acepromazine and atropine and during subsequent general anesthesia and surgery. *Am J Vet Res* 1992;53:2067–2070.
7. Wagner AE, Muir WW, Hinchcliff KW. Cardiovascular effects of xylazine and detomidine in horses. *Am J Vet Res* 1991;52:651–657.
8. Figueiredo JP, Muir WW, Smith J, et al. Sedative and analgesic effects of romifidine in horses. *Int J Appl Res Vet Med* 2005;3:249–258.
9. Lavoie JP, Pascoe JR, Kurpershoek CJ. Effect of head and neck position on respiratory mechanics in horses sedated with xylazine. *Am J Vet Res* 1992;53:1652–1657.
10. Trim CM, Hanson RR. Effects of xylazine on renal function and plasma glucose in ponies. *Vet Rec* 1986;118:65–67.
11. Rutkowski JA, Ross MW, Cullen K. Effects of xylazine and/or butorphanol or neostigmine on myoelectrical activity of the cecum and right ventral colon in female ponies. *Am J Vet Res* 1989;50:1096–1101.
12. Schatzmann U, Josseck H, Stauffer JL, et al. Effects of α-2 agonists on intrauterine pressure and sedation in horses: comparison between detomidine, romifidine, and xylazine. *J Vet Med* 1994;41:523–529.
13. Luukkanen L, Katila T, Koskinen E. Some effects of multiple administrations of detomidine during the last trimester of equine pregnancy. *Equine Vet J* 1997;29:400–403.
14. Hoffman PE. Clinical evaluation of xylazine as a chemical restraining agent, sedative, and analgesic in horses. *J Am Vet Med Assoc* 1974;164:42–45.
15. Peters DF, Erfle JB, Slobojan GT. Aggressive behavior associated with the use of xylazine and detomidine, in *Proceedings*. 44th Annual American Association of Equine Practitioners Convention 1998;294–286.
16. Robertson JT, Muir WW. A new analgesic drug combination in the horse. *Am J Vet Res* 1983;44:1667–1669.
17. Brunson DB, Majors LJ. Comparative analgesia of xylazine/morphine, xylazine/butorphanol, and xylazine/nalbuphine in the horse, using dental dolorimetry. *Am J Vet Res* 1987;48:1087–1091.
18. Freeman SL, England CG. Investigation of romifidine and detomidine for the clinical sedation of horses. *Vet Rec* 2000;147:507–511.
19. Taylor PM, Rymaszewska H, Young SS. Evaluations of combinations of nalbuphine with acepromazine or detomidine for sedation in ponies. *J Assoc Vet Anaesth Gr Brit Ire* 1990;17:38–41.
20. Van Dijk P, Lankveld DPK, Rijkenhuizen ABM, et al. Hormonal, metabolic and physiological effects of laparoscopic surgery using a detomidine-buprenorphine combination in standing horses. *Vet Anaesth Analg* 2003;30:71–79.

21. Taylor PM, Browning AP, Harris CP. Detomidine-butorphanol sedation in equine clinical practice. *Vet Rec* 1988;123:388–390.

22. Hamm D, Turchi P, Jochle W. Sedative and analgesic effects of detomidine and romifidine in horses. *Vet Rec* 1995;136:324–327.

23. England GCW, Clarke KW, Goosens L. A comparison of the sedative effects of three α-2 adrenoceptor agonists (romifidine, detomidine and xylazine) in the horse. *J Vet Pharmacol Ther* 1992;15:194–201.

24. Spadavecchia C, Arendt-Nielsen L, Anderson OK, et al. Effect of romifidine on the nociceptive withdrawal reflex and temporal summation in conscious horses. *Am J Vet Res* 2005;66:1992–1998.

25. Bueno AC, Seahorn JC, Seahorn TL, et al. Cardiopulmonary and sedative effects of intravenous administration of low doses of medetomidine and xylazine to adult horses. *Am J Vet Res* 1999;60:1371–1376.

26. Yamashita K, Tsubakishita S, Futaoka S, et al. Cardiovascular effects of medetomidine, detomidine and xylazine in horses. *J Vet Med Sci* 2000;62:1025–1032.

27. Ramsay EC, Geiser D, Carter W, et al. Serum concentrations and effects of detomidine delivered orally to horses in three different mediums. *Vet Anaesth Analg* 2002;29:219–222.

28. Freeman SL, England GCW. Comparison of sedative effects of romifidine following intravenous, intramuscular, and sublingual administration to horses. *Am J Vet Res* 1999;60:954–959.

29. Goodrich LR, Clark-Price S, Ludders J. How to attain effective and consistent sedation for standing procedures in the horse using constant rate infusion, in *Proceedings*. 50th Annual American Association of Equine Practitioners Convention 2004;229–232.

30. Robertson JT, Muir WW, Sams RA. Cardiopulmonary effects of butorphanol tartrate in horses. *Am J Vet Res* 1981;42:41–44.

31. Sellon DC, Roberts MC, Blikslager AT, et al. Effects of continuous rate intravenous infusion of butorphanol on physiologic and outcome variables in horses after celiotomy. *J Vet Int Med* 2004;18:555–563.

32. Clarke KW, Paton BS. Combined use of detomidine with opiates in the horse. *Equine Vet J* 1988;20:331–334.

33. Corletto F, Raisis AA, Brearley JC. Comparison of morphine and butorphanol as pre-anesthetic agents in combination with romifidine for field castration in ponies. *Vet Anaesth Analg* 2005;32:16–22.

34. Muir WW, Skarda RT, Sheehan WC. Hemodynamic and respiratory effects of xylazine-morphine sulfate in horses. *Am J Vet Res* 1979;40:1417–1420.

35. Matthews NS, Fielding CL, Swinebroad H. How to use a ketamine constant rate infusion in horses for analgesia, in *Proceedings*. 50th Annual American Association of Equine Practitioners Convention 2004;227–228.

36. Lankveld DPK, Driessen D, Soma L, et al. Pharmacodynamic effects and pharmacokinetic profile of a long-term continuous rate infusion of racemic ketamine in healthy conscious horses. *J Vet Pharmacol Ther* 2006;29:477–488.

37. Fielding CL, Brumbaugh GW, Matthews NS, et al. Pharmacokinetics and clinical effects of a subanesthetic continuous rate infusion of ketamine in awake horses. *Am J Vet Res* 2006;67:1484–1490.

38. Doherty TJ, Frazier DL. Effect of intravenous lidocaine on halothane minimum alveolar concentration in ponies. *Equine Vet J* 1998;30:300–303.

39. Robertson SA, Sanchez LC, Merritt AM, et al. Effect of systemic lidocaine on visceral and somatic nociception in conscious horses. *Equine Vet J* 2005;37:122–127.