

Review of Equine Analgesics and Pain Management

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Many drugs and administration techniques are now available to the veterinarian for the management of equine pain. Balancing the use of drugs that act at different locations or by different mechanisms in the pain pathway improves analgesia, minimizes cost, and lessens side effects. Providing good analgesia improves the patient's recovery and shortens hospital stays, thus improving outcome. Authors' address: Department of Veterinary Small Animal Clinical Sciences, Texas A&M University, 4474-TAMU, College Station, TX 77843-4474; e-mail: nmatthews@cvm.tamu.edu. © 2007 AAEP.

1. Introduction

Pain is very debilitating in the horse and may be primarily responsible for the result of euthanasia during certain medical conditions (e.g., laminitis). Yet, adequate pain management may be expensive, difficult to evaluate, and may require frequent drug administration. Additionally, most commonly used analgesics (i.e., non-steroidal anti-inflammatory drugs [NSAIDs]) come with their own set of limiting side effects.

Positive benefits of analgesia include maintenance of weight, shorter hospitalizations, and lower total patient bills.¹ The use of analgesics in horses grows as the complexity of surgical treatment increases. Because equine pain management is a large topic, this review will focus on pain management during the perioperative period. The drugs and techniques used in perioperative pain management are also useful in chronic conditions.

2. The Concept of Balanced Analgesia

The concept of balanced (or multimodal) analgesia is to use a variety of drugs that have different modes of

action or that act on different receptor types; these drugs are used to provide good analgesia with lower dosages of each drug, which decreases possible side effects. The simplest (yet widely used) combination of an α_2 -agonist (e.g., xylazine) for sedation, local anesthetic block, and an NSAID provides balanced or "multimodal" analgesia.

A multitude of such combinations may be formulated depending on patient need and intended route of administration. Currently, many drugs may be administered parenterally (e.g., IV, IM, or SC) as well as orally (PO). Regional local anesthetic blocks (e.g., intra-articular [IA], epidural, four-point, etc.), transdermal (TD), and transmucosal (TM) are other routes that may be used. Constant-rate infusions (CRIs) of IV drugs allow for consistent blood concentration with overall lower doses; thus, there are fewer side effects.

3. Methods of Administration

The usual routes of administration (IV, IM, SC, epidural injections, and PO) are all very useful, but newer analgesics can be administered transder-

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mally by patch or topical application. CRIs allow for the IV administration of lower doses (fewer side effects) to maintain consistent plasma concentrations, which produces analgesia with fewer peaks and troughs. Many drugs may be administered by multiple methods depending on the method that is most practical for the patient. An analgesic regimen might combine different drugs given by different routes, which could help to reduce injection pain or adverse gastrointestinal side effects and improve owner compliance.

4. NSAIDs

Several different NSAIDs (phenylbutazone,^a flunixin,^b and ketoprofen^c) have been widely and effectively used for pain management in horses. However, all have the potential to produce significant side effects, especially when used at high doses. Although not approved for use in horses in the United States, the newer NSAIDs like meloxicam^d (0.6 mg/kg, IV) and carprofen^e (0.7 mg/kg, IV) may have fewer side effects with good efficacy. Transdermal 1% diclofenac^f may have the advantage of decreased side effects, because it can be used on the specific site where analgesia is required. Because all are fairly similar, the choice of NSAID is likely to depend on availability and cost. Individual patients may vary in their response to a particular NSAID (much as occurs in humans), and this may also affect the choice of drug to use for a particular patient. Although NSAIDs are very effective for pain reduction in horses, it is unlikely that they will produce sufficient analgesia for severely painful conditions; however, it should be a basic “building block” of balanced analgesia. The veterinarian must also remember that severe or chronic pain is very difficult to treat; it may be “refractory” to analgesics that normally are quite effective. Chronic pain requires aggressive and multimodal analgesia for successful treatment. Reasonable outcome expectations for analgesia may need to include feed consumption and mobility rather than a complete return to normal weight bearing.

5. Opioid Analgesics

Opioids have been a mainstay of pain relief in both the human and veterinary field. The usefulness of opioids as single-agent analgesics in horses has been tempered by the propensity for opioids to produce excitement when administered alone in non-painful horses. Gastrointestinal stasis may also occur in some horses. Morphine^g (0.1 mg/kg, IV or IM), meperidine^h (4.4 mg/kg, IV or IM), methadoneⁱ (0.22 mg/kg, IV), and oxymorphone^j (0.033 mg/kg, IV) have all been used alone for analgesia and with sedatives to facilitate standing surgery.

Butorphanol^k (schedule IV; 0.01–0.1 mg/kg, IV or IM), an agonist-antagonist opioid approved for use in the horse in the United States, has also been widely used for analgesia and sedation in conjunction with α_2 -agonists. Although the degree of analgesia

provided by butorphanol has been questioned, it has become widely used in equine medicine, particularly before being scheduled. Nalbuphine^l is another agonist-antagonist opioid (much like butorphanol) that currently has the advantage of not being a scheduled drug. Nalbuphine (0.3 mg/kg, IV) has been evaluated with detomidine^m (0.01 mg/kg, IV) or acepromazineⁿ (0.05 mg/kg, IV), and it produced good sedation with both; however, the analgesic effect was not evaluated.² Analgesia (dental dolorimetry model) was evaluated with nalbuphine (0.75 mg/kg, IV) and compared with morphine, butorphanol, and xylazine.^{o3} No difference between groups was seen. Nalbuphine is less potent and efficacious than butorphanol, but it has been used for analgesia, especially in countries where other opioids are not available.

Buprenorphine^p (0.004–0.006 mg/kg, IV, IM, or SC) has the advantage of a long duration of action (6–8 h), but it is not approved for equine use (or any veterinary use). Buprenorphine (q 8 h) has been used in the multimodal analgesic management of laminitis. The TM or PO absorption of buprenorphine has not been reported in horses. In cats, TM buprenorphine is 100% bioavailable. A transdermal form of buprenorphine is available in the United Kingdom^q and Australia.^r

Fentanyl^s is a short-acting, μ -receptor opioid that produces increased locomotor activity in horses, an effect that is similar to the earlier opioid studies that were reported by Tobin et al.^{4,5} Transdermal fentanyl^t (fentanyl patches are now generic) is not approved for use in horses but has been used for analgesia. Uptake of transdermal fentanyl is more rapid in the horse; blood levels consistent with analgesia are present within 4 h of application compared with 12 h in humans and small animals.⁶ Two 100-mcg/h patches for a 450-kg horse are the typical dose. The two patches may be applied to a clipped area of the skin and bandaged in place to insure good skin contact. Because it is easy to place a bandage on the forearm or gaskin, these locations are easy sites to use.

Although patches are supposed to provide analgesia for 72 h in people, reapplication at 48 h should be considered depending on response and reevaluation of pain. Systemic fentanyl (1–4 mcg/kg/h) has been used in conjunction with inhalant anesthesia to reduce the vaporizer setting required. However, when alfentanil^u was used with halothane, no minimum alveolar concentration (MAC)-sparing effect was seen in horses, so further research is needed to determine if these drugs are beneficial when used with inhalant anesthesia.⁷ Fentanyl is also a potent respiratory depressant, and mechanical ventilation is required when it is used with inhalant anesthesia.

Tramadol,^v a non-opiate μ -agonist for the treatment of mild to moderate pain, has the advantage that it is not currently a scheduled drug. In addition to other drug activity, tramadol has analgesic

activity similar to μ -agonists; morphine is the gold standard for μ -opioid activity). Tramadol is also a serotonin-reuptake inhibitor, and it lowers the seizure threshold in people. Tramadol is not approved for veterinary use, but it is used extensively to treat mild to moderate pain in dogs and cats. Although the efficacy of tramadol has not been documented in horses, the pharmacokinetics of oral (10 mg/kg) and IV (4 mg/kg) dosing have been reported in foals.⁸ Further investigation is needed for this promising drug, especially because the cost has decreased since it became available in generic form.

6. Alpha₂-Agonists

Xylazine, detomidine, romifidine,^w and medetomidine^x have all been used to produce sedation and analgesia by different routes (IV, IM, and PO) and different injection techniques (periodic bolus versus CRI). These are versatile drugs, and they have been used by epidural and IA injection to produce analgesia.⁹ Intra-operative detomidine CRI (0.18 mcg/kg/min) can be used to decrease inhalant anesthesia by ~30%.¹⁰ Medetomidine (7 mcg/kg, initial bolus followed by 3.5 mcg/kg/h, IV) has been used to produce a 28% inhalant MAC -sparing effect in horses.¹¹

7. Local Anesthetics

No discussion of analgesics would be complete without including local anesthetics, which can also be

used in a variety of ways: local infiltration, anatomic nerve block, regional limb block or perfusion, epidural, and CRI. Although lidocaine^y and mepivacaine^z produce a short duration of action, bupivacaine^{aa} offers the advantage of lasting for 6–8 h. Although more toxic (dose should be limited to 2 mg/kg), bupivacaine may be used as a regional block (e.g., pastern arthrodesis) intra-operatively and will last into the post-operative period. Local anesthetic blocks (e.g., blocking the testicle during a castration or “splash blocking” ovarian pedicle during ovariectomy) may be used in conjunction with injectable or inhalant anesthesia to provide analgesia and decrease the MAC value needed (i.e., allow for lower vaporizer settings to be used).

Epidural analgesia or anesthesia (e.g., morphine, bupivacaine, or combination) may be very useful. Caution must be used when administering an epidural in awake horses to protect against the excessive ataxia produced by the cranial migration of the local anesthetic. Ropivacaine^{bb} is a newer, longer-acting local anesthetic with a higher affinity for pain versus motor fibers; therefore, ataxia is less likely to occur. It has been used epidurally (0.08–0.1 mg/kg in a total volume of 8–9 ml) for standing surgery.¹²

CRIs of lidocaine have been shown to decrease inhalant anesthetic requirements by 25% (isoflurane)¹³ and 30–50% (halothane).¹⁴ This may contribute to maintaining better blood pressures intra-operatively, since the vaporizer setting can be

Table 1. Analgesic Drugs for Treatment of Pain in Horses (See Text for Doses for CRIs)

| Drug | Dose (mg/kg) | Route | Indications | Duration of Action | Side Effects |
|--|--------------|-------------|------------------------|--------------------|-----------------------------------|
| <i>Alpha-two agonists</i> | | | | | |
| Xylazine | 0.17 | epidural | caudal analgesia | short | ataxia, bradycardia |
| Detomidine | 0.02–0.03 | epidural | caudal analgesia | long | ataxia |
| <i>Non-steroidal antiinflammatories</i> | | | | | |
| Phenylbutazone | 2–4 | IV | relief of inflammation | 24 hrs | GI ulcers |
| Flunixin meglumine | 1.1 | IV | relief of inflammation | 24 hrs | GI ulcers |
| Ketoprofen | 2.2 | IV | relief of inflammation | 24 hrs | GI ulcers |
| Carprofen | 0.7 | IV | relief of inflammation | 24 hrs | GI ulcers |
| Meloxicam | 0.6 | IV | relief of inflammation | 24 hrs | GI ulcers |
| <i>Opioid analgesics:mu-receptor agonists</i> | | | | | |
| Morphine | 0.1 | IV, IM | severe pain | short | respiratory depression, GI stasis |
| Meperidine | 4.4 | IV, IM | severe pain | short | respiratory depression, GI stasis |
| Fentanyl | 20 mg Total | transdermal | moderate pain | 48 hrs | respiratory depression, GI stasis |
| Methadone | 0.22 | IV | moderate pain | short | respiratory depression, GI stasis |
| Oxymorphone | 0.033 | IV | severe pain | short | respiratory depression, GI stasis |
| <i>Opioid analgesics: partial receptor agonists or antagonists</i> | | | | | |
| Butorphanol | 0.01–0.1 | IV, IM, SC | mild pain | short | respiratory depression, GI stasis |
| Nalbuphine | 0.3 | IV | mild pain | short | respiratory depression, GI stasis |
| Buprenorphine | 0.004–.006 | IV, IM, SC | moderate pain | long | respiratory depression, GI stasis |
| <i>Other analgesics</i> | | | | | |
| Ketamine | 0.4–0.8/hr | IV | moderate pain | use in CRI | CNS excitation |
| Tramadol | 4–10 | oral | moderate pain | short | GI stasis |
| Methocarbamol | 4–25 | IV | ms. Relaxation | 6 hrs | CNS depression |

lowered. Lidocaine CRIs have also been used for their prokinetic activity, especially in post-operative colics. An initial bolus of 1.3 mg/kg lidocaine, given over 15 min, is followed by 3 mg/kg/h.¹⁵

8. Epidural Analgesia

Epidural analgesia may be achieved with maintenance of motor function by using morphine (0.1 mg/kg), ketamine^{cc} (0.2–2 mg/kg), or tramadol (1 mg/kg). Xylazine (0.17 mg/kg) and detomidine (0.02–0.03 mg/kg) have been used alone or in combination with other drugs for epidural analgesia.¹⁶ Drugs may be administered as a single bolus or injection into an epidural catheter. An epidural catheter may be placed and maintained for long periods of time, which allows for intermittent administration through the catheter.

9. Other CRIs

Ketamine (0.4–0.8 mg/kg/h, IV) has been used for fairly prolonged administration with no appreciated side effects. Ketamine is very effective for patients with somatic pain (e.g., burns) and has been used for septic arthritis. “Three-legged lame” patients did not miraculously become sound during the infusions, but appetite increased, and the horses seemed more comfortable. Ketamine is less likely to decrease gastrointestinal motility than the opioids. Ketamine may also be used in conjunction with other drugs (e.g., lidocaine or butorphanol), because they all work on different receptor sites.

Butorphanol infusions (13 mcg/kg/h, IV) provide analgesia for post-operative colics. Butorphanol-treated horses had shorter hospital stays and better appetites.

Detomidine or medetomidine CRIs may be used to facilitate standing surgeries while keeping the sedation at a consistent level. Different publications have presented different “recipes” for detomidine.^{17,18} Detomidine has a relatively long half-life and will accumulate over time unless the dose is reduced. Accumulation of detomidine will lead to increasing depths of sedation and long recovery from sedation. Medetomidine has also been used by CR I for standing surgery (5 mcg/kg, IV initial bolus followed by 3.5 mcg/kg/hr, IV for 2 h).¹⁹

Medetomidine also has a fairly long duration of action, and reduction of the dose toward the end of the procedure is advised to prevent excessive sedation.

10. Other Therapies?

Muscle relaxants (methocarbamol^{dd}) may be useful adjuncts to other analgesics for certain painful conditions in horses, and they could be a component of balanced analgesia.

Although there is little proof of the benefit of massage, acupuncture, laser therapy, and other complementary therapies, they may all prove to help in optimizing analgesic regimens.

11. Summary

There are many drugs and techniques that may be used to provide analgesia for the equine patient. Combinations of different drugs (balanced or multimodal analgesia) seem to be most effective in providing pain relief while minimizing adverse side effects. Because each patient's pain is likely to be different, no one “recipe” is appropriate for all patients; the veterinarian is encouraged to “customize” drugs based on the patient's response.

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- ^bBanamine, Schering Plough Animal Health, Summit, NJ 07901.
- ^cKetoprofen, Fort Dodge Animal Health, Fort Dodge, IA 50501.
- ^dMetacam, Boehringer Ingelheim Vet Medica, St. Joseph, MO 64506.
- ^eRimadyl injectable, Pfizer Animal Health, Exton, PA 19341.
- ^fSurpass cream, IDEXX Labs, Westbrook, ME 04092.
- ^gMorphine sulfate injection, Baxter Healthcare Corp., Deerfield, IL 60015.
- ^hMeperidine HCl injection, Elkins-Sinn Inc., Cherry Hill, NJ 08003.
- ⁱDolorphone Injection, Roxane Labs Inc., Columbus, OH 43228.
- ^jNumorphan HCl, Endo Pharm Inc., Chadds Ford, PA 19317.
- ^kTorbagesic, Fort Dodge Animal Health, Fort Dodge, IA 50501.
- ^lNalbuphine hydrochloride injection, Hospira Inc., Lake Forest, IL 60045.
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- ⁿAcepromazine maleate injection, Vedco Inc., St. Joseph, MO 64507.
- ^oAnased, Lloyd Labs, Shenandoah, IA 51601.
- ^pBuprenorphine hydrochloride injection, Bedford Labs, Bedford, OH 44146.
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- ^rNorspan, Mundipharma Pty. Ltd., Sydney 2059, NSW, Australia.
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