Anesthesia and Analgesia for Standing Equine Surgery

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Anesthesia and Analgesia for Standing Equine Surgery

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KEYWORDS

- Standing equine surgery
- Equine Anesthesia
- Standing sedation
- Epidural equine analgesia
- Epidural catheterization

INTRODUCTION

The risks associated with equine anesthesia are well known to any professional involved in equine medical care. It has been repeatedly shown that general anesthesia in horses has the highest complication rate of any other domestic species. An anesthetic-related mortality of up to 1\% for elective procedures, and 10\% for emergency procedures, has been reported.\textsuperscript{1–3} These worrisome data should always be kept in mind when contemplating whether the benefit of general anesthesia for a specific patient and procedure outweighs the risks. However, considering mortality alone significantly underestimates the overall morbidity of equine anesthesia in terms of nonlethal injuries occurring during recovery.\textsuperscript{4} The astronomically high complication rate seems to be mainly due to the cardiovascular and respiratory alterations caused...
by anesthesia and recumbency. Decreased tissue perfusion and oxygenation to the muscles and visceral organs are also responsible for the development of myopathy and gastrointestinal dysfunction.

The development and practice of sedative protocols that would allow the practitioner to perform diagnostic and surgical procedures with the patient remaining standing would therefore be ideal in certain circumstances. Sedation maintains the physiologic cardiovascular compensatory mechanisms that are commonly depressed during general anesthesia. Maintaining the horse in a standing position also has the absolute advantage over general anesthesia of eliminating the detrimental effect of recumbency on gas exchange and muscle perfusion.

However, the physiologic advantages of standing sedation are counterbalanced by the inherent difficulties of maintaining appropriate patient restraint for the surgical procedure. Excessive sedation and muscle relaxation would induce tremors, ataxia, or worse, causing the animal to fall. A plane of sedation that is too superficial instead would potentially induce delirium and hypersensitivity to stimulation. In this regard, the use of short-acting sedatives because titrated continuous infusion seems to be preferable over bolus dosing of longer-acting agents. Infusion of short-acting agents allows the achievement of the wanted effect and the titration to a steady state of sedation in a more rapid fashion. Bolus dosing alone instead will likely produce intermittent peaks and troughs of levels of sedation and possibly higher risk of over- or undersedation. The use of continuous infusions would likely provide a more constant sedative effect once the initial loading bolus has been administered.

The combination of drugs with different pharmacologic action allows for reduced doses of individual drugs, thereby decreasing their side effects. A balanced approach by supplementing sedatives and tranquilizers with systemic analgesic or regional anesthetic techniques facilitates standing procedures. Multimodal analgesia would also provide superior analgesia with potentially fewer side effects than a single-agent approach.

Although standing sedation is widely recognized to be associated with a lower risk of severe complications compared with general anesthesia, the current literature is lacking in precise indications in regard to the complication rate and mortality. Due to the lack of definitive evidence of superiority of one sedative protocol over another, the management of standing sedation in horses is still based on tradition, personal bias, and institutional preference rather than on scientific approaches.

Nevertheless, a critical consideration is related to the safety of the staff. The safety of the personnel involved in the procedure represents the most important factor to consider when approaching a procedure under standing sedation in horses. In this regard, the margin of error becomes much narrower than during general anesthesia and the anesthetist has the responsibility, not only to ensure the highest level of anesthetic care to the patient but also to provide a safe and protected working condition for the operators involved.

PATIENT ASSESSMENT AND PREPARATION

Dr Robert Moors Smith, an icon of human pediatric anesthesiology, when asked an opinion about what is the role of his profession in modern medicine, briefly answered: “There are no safe anesthetic agents, there are no safe anesthetic procedures, there are only safe anesthetists.” This statement brilliantly summarizes the critical importance of the appropriate selection and direct supervision of any sedated or anesthetized patient. Preliminary examination, appropriate patient stabilization, and
intraprocedural monitoring by the anesthetist are compulsory to performing a safe and uneventful standing sedation.

Patient selection is the first step for a successful standing procedure. Fractious or highly stressed horses are unlikely to tolerate any manual restraining and handling. It is notorious that highly sympathetically driven animals appear to be resistant to standard doses of sedatives. However, unpredictable oversedation may result with the use of higher dosages. Therefore for these reasons and because of the potential risk for the personnel involved, these patients should be considered poor candidates for standing sedation.

“Plan for the worst!” is a general rule for any sedation or anesthesia in horses. When planning for a standing procedure, it is critical to anticipate the possible occurrence of complications to be prepared for a prompt intervention. For example, a major risk of standing sedation is the falling of the patient on the ground. In this unfortunate scenario, the recommended intervention is a rapid induction of general anesthesia and placement of the patient in an appropriately padded stall for recovery. Therefore, it is indicated to always calculate and have available appropriate doses of induction agents (ie, ketamine and diazepam). In addition, endotracheal tubes of different sizes and oxygen supply should be available in case of a need for rapid intubation after induction of anesthesia. All equipment and emergency medications should be prepared in advance to ensure appropriate intervention under emergency conditions.

As part of the patient’s preparation, an intravenous catheter should be placed for drugs and fluid administration, and the horse’s mouth should be washed in case there is a need for endotracheal intubation. For prolonged procedures (>1 hour), the placement of a urinary catheter is recommended for urine collection, especially when α2-agonists are used. The aim is to prevent the spread of urine on the floor that could increase the risk of accidental fall of the animal.

A quiet location, devoid of stimulating factors such as bright light, noise, and other horses, should be chosen for the procedure. Use of blinders and placing swabs in the ears once the patient is sedated help to reduce stimulation. For prolonged procedures, the use of a dedicated room, equipped with specific stocks to confine the horse, is highly recommended. Fully walled stocks should be avoided. The stocks should be constructed of metal bars only to leave free access to the animal from all sides.

Indications for standing sedation must consider the complexity and duration of the procedure. Complexity of the surgical procedure has been associated with the risk of anesthetic-related complications.1 Increasing duration also, independently from the type of surgical procedure, was associated with increased risk.1 These principles would likely also apply to standing sedation. Prolonged procedures expose the patient to drug accumulation, increased risk of undesired effects, and prolonged recovery. Therefore, the practitioner’s familiarity with the procedure and the experience of the personnel involved in the procedure play an important role at decreasing the risk of complications.2

With appropriate sedation and analgesia, there are several procedures that can be performed in the standing conscious horse. Diagnostic procedures, such as magnetic resonance imaging, scintigraphy, and endoscopy, usually require minimal or no analgesia, whereas invasive surgical interventions may require a multimodal approach to control pain.

Minor surgical procedures, which are often considered for standing sedation, include tracheostomy, placement of a subpalpebral lavage system, tarsorrhaphy, removal of the nictitating membrane, and cryosurgery for removal of small cutaneous masses.

Sinus surgery, excision of large cutaneous masses, thoracoscopy, and laparascopy are examples of more invasive indications for standing sedation in which appropriate analgesia is critical for successful results. Standing laparoscopy is commonly used for
diagnostic biopsy, ovariectomy, cryptorchidectomy, and colopexy. Perineal surgery and urethral surgery are other common indications for standing sedation. The standing position in these cases maintains the symmetry of the anatomic landmarks, hence facilitating the surgical approach. Profound analgesia for perineal surgery can be successfully provided with regional techniques such as epidural analgesia and a pudendal nerve block. The combination of these analgesic techniques with the sedation protocol would significantly reduce nociceptive stimulation and the risk of unwanted reactions of the patient. Other procedures performed in the standing position are included in later articles within this issue.

PHARMACOLOGY

Ideal drug combinations for standing procedures should provide reliable sedation, cause minimal ataxia, and provide adequate analgesia. Virtually all of these combinations include $\alpha_2$-agonists along with another agent with synergistic effect. Following is a description of some recommended protocols with relative duration of effect and practical indications for use.

**Acepromazine**

Acepromazine is commonly used for premedication. It is very effective as an anxiolytic; however, it provides only a mild to moderate degree of sedation. Acepromazine at the dose of 0.02 to 0.04 mg/kg can provide sufficient restraint for clipping and placement of an intravenous catheter. The intramuscular route of administration is associated with a delay in the peak sedative effect of about 30 to 45 minutes. With intravenous injection, the sedative effect is achieved usually within 15 minutes. The duration of sedation is 3 to 4 hours. Acepromazine does not provide any analgesic effect. Occasionally paradoxic excitement may occur. Acepromazine provides a good calming effect, and it significantly decreases the requirements of other sedatives used in combination. In horses it also has antiarrhythogenic properties. If profound sedation is needed, acepromazine alone is likely to be insufficient even at high doses. Increasing the dose will only increase the duration of action, without further increasing the intensity of sedation. For this reason, it should always be used in combination with other drugs, such as $\alpha_2$-agonists and opioids.

Acepromazine can cause sudden collapse in excited horses, although this occurrence is extremely rare. The suggested mechanism for this overresponse is that sympathetically driven animals have high circulating levels of catecholamines. Circulating epinephrine preferentially acts at $\beta$-adrenergic receptors, causing skeletal muscle vasodilation and, as peripheral $\alpha_1$-receptors are blocked by acepromazine, this will unmask the vasodilation, with secondary profound hypotension and possible collapse. Acepromazine is not suitable for use in hypovolemic or septic patients, because drug-induced vasodilatation will worsen the preexisting cardiovascular instability. Acepromazine is contraindicated in breeding stallions, because it has been associated with priapism and paraphimosis, although this has been proven to be extremely rare.

**$\alpha_2$-Agonists**

$\alpha_2$-Adrenoreceptor agonists are undoubtedly the main-stem component of any standing sedation in horses. It is realistically impossible to provide a reliable, stable, and profound degree of sedation without using an $\alpha_2$-adrenoreceptor agonist. Xylazine, romifidine, detomidine, and dexmedetomidine are available for use in horses. Their peak effect occurs approximately 2 to 5 and 15 to 30 minutes after intravenous and intramuscular administration, respectively. The intramuscular dose required to
produce similar intensity of sedation is approximately double the intravenous dose for all of the agents belonging to this class.

Recently, the pharmacokinetics and pharmacodynamics of a detomidine gel administered sublingually have been investigated. At the dose of 0.04 mg/kg, mild to moderate sedation was observed. The time of onset of sedation was about 40 minutes, and duration was approximately 2 hours. Large interindividual variability of effect was observed.12

All $\alpha_2$-agonists produce reliable, sedative, visceral, and somatic analgesic, and muscle-relaxant effects.13 $\alpha_2$-Agonists are characterized by a “ceiling” sedative effect, whereby increasing the dose extends the duration but does not increase the intensity of sedation.14 After the initial bolus, there are 2 options to maintain sedation for prolonged procedures. Supplemental intravenous doses can be given as needed when the sedative effects start decreasing, at approximately one-quarter to one-half of the initial dose. Alternatively, many authors recommend the administration as continuous intravenous infusions, avoiding the “peaks and troughs” seen with repeat bolus injections.

Common side effects of all $\alpha_2$-agonists include bradycardia, second-degree atrioventricular block, biphasic hypertension followed by hypotension, increased urine production, moderate hyperglycemia, sweating, and decreased gastrointestinal motility.10 Ataxia appears more profound with xylazine compared with romifidine or detomidine.15 Increased myometrial contractility and intrauterine pressure have been shown to occur with xylazine; therefore, it should not be used during the last trimester of pregnancy. Conversely, detomidine has been shown to reduce intrauterine pressure, and therefore, it represents the sedative of choice in pregnant mares at late stages of pregnancy.16

The intravenous administration of detomidine was also shown to decrease intraocular pressure in clinically normal horses and may represent a safe sedative when performing ocular procedures.17

$\alpha_2$-Agonists given as a bolus cause a temporary increase in afterload with secondary depression of ventricular function and cause myocardial hypoxia due to coronary vasoconstriction. The magnitude of these effects appears to be largely dose independent and is demonstrated by the near-maximal magnitude of cardiovascular changes occurring even at microdoses of these agents. Therefore the use of “low doses” should not be considered safer than high doses. Instead, the preliminary evaluation and appropriate patient selection are the most important factors in determining the safety of the use of any $\alpha_2$-agonist.18

The solution for a continuous infusion can be prepared by adding the selected $\alpha_2$-agonist agent to a bag of isotonic crystalloid fluids. This solution is initially administered at a calculated drip rate and then titrated to effect on a case-by-case basis. Bolus doses and infusion rates for many $\alpha_2$-agonists have been investigated for standing sedation in horses. The duration of sedation is longest with romifidine, followed by detomidine, dexmedetomidine, and xylazine, when equipotent intravenous doses are used.19 The recommended infusion rates should be adjusted based on the patient response and the level of sedation required. The combination of any $\alpha_2$-agonist with butorphanol also allows the reduction of the infusion rate to up to one-half of the rate of the drug used alone.20,21

Recommended bolus doses and infusion rates are listed below and reported in Table 1:

- Xylazine: The recommended bolus is 0.8 to 1 mg/kg followed by an infusion rate of 0.65 mg/kg/h. Significant ataxia has been shown at high doses and with prolonged infusions.20
Romifidine: The initial recommended dose is 0.1 mg/kg followed by 0.03 mg/kg/h.\textsuperscript{21} The time to maximal sedation and complete recovery is longer with romifidine than with other α2-agonists. The onset of sedation is 5 to 10 minutes after intravenous bolus and the duration of effect is about 60 minutes.\textsuperscript{22}

Detomidine: An initial bolus of 0.01 mg/kg intravenously can be followed by an infusion of 0.01 to 0.04 mg/kg/h.\textsuperscript{23,24} At the high-dose range, ataxia is a common occurrence. When higher infusion rates are required for extended periods of time to maintain an adequate level of sedation, combination with other agents is recommended. The authors commonly use a standard bolus of 0.01 mg/kg followed by an infusion at 0.03 mg/kg/h. If the degree of sedation achieved at this rate does not meet the requirement for the procedure, the addition of butorphanol is then indicated. The combination of butorphanol with detomidine produces a potent synergistic effect. Individual constant rate infusion (CRI) doses should be halved to avoid oversedation.\textsuperscript{25}

Dexmedetomidine is the most potent agent among the commercially available α2-agonists. A bolus of 0.003 to 0.005 mg/kg intravenously has been used by the authors for standing sedation of brief duration (<30 minutes). For longer procedures, an infusion at 0.005 mg/kg/h is indicated. After bolus administration, dexmedetomidine has been shown to produce cardiopulmonary changes similar to other α2-agonists, but of very short duration. Pharmacokinetic studies of dexmedetomidine in horses showed rapid distribution and rapid clearance. These pharmacokinetic characteristics favor its use as a CRI.\textsuperscript{26} The cost of the drug, however, still represents the major obstacle to the routine use of dexmedetomidine in equine sedation.

The intravenous solutions of α2-agonists for infusion for a 450-kg horse can be prepared by the following:

- 400 mg xylazine added to a 500-mL bag of saline (0.8 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.65 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.3 mg/kg/h)
- 20 mg romifidine added to a 500-mL bag of saline (0.04 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.03 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.015 mg/kg/h)
- 25 mg of detomidine added to a 500-mL bag of saline (0.05 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides

<table>
<thead>
<tr>
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</tr>
<tr>
<td>Romifidine</td>
<td>Bolus: 0.1 mg/kg CRI: 0.03 mg/kg/h</td>
</tr>
<tr>
<td>Detomidine</td>
<td>Bolus: 0.01 mg/kg CRI: 0.01–0.04 mg/kg/h</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Bolus: 0.003–0.005 mg/kg CRI: 0.005 mg/kg/h</td>
</tr>
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</table>

Table 1

Recommended intravenous boluses and CRI for α2-agonists

- Romifidine: The initial recommended dose is 0.1 mg/kg followed by 0.03 mg/kg/h.\textsuperscript{21} The time to maximal sedation and complete recovery is longer with romifidine than with other α2-agonists. The onset of sedation is 5 to 10 minutes after intravenous bolus and the duration of effect is about 60 minutes.\textsuperscript{22}

- Detomidine: An initial bolus of 0.01 mg/kg intravenously can be followed by an infusion of 0.01 to 0.04 mg/kg/h.\textsuperscript{23,24} At the high-dose range, ataxia is a common occurrence. When higher infusion rates are required for extended periods of time to maintain an adequate level of sedation, combination with other agents is recommended. The authors commonly use a standard bolus of 0.01 mg/kg followed by an infusion at 0.03 mg/kg/h. If the degree of sedation achieved at this rate does not meet the requirement for the procedure, the addition of butorphanol is then indicated. The combination of butorphanol with detomidine produces a potent synergistic effect. Individual constant rate infusion (CRI) doses should be halved to avoid oversedation.\textsuperscript{25}

- Dexmedetomidine is the most potent agent among the commercially available α2-agonists. A bolus of 0.003 to 0.005 mg/kg intravenously has been used by the authors for standing sedation of brief duration (<30 minutes). For longer procedures, an infusion at 0.005 mg/kg/h is indicated. After bolus administration, dexmedetomidine has been shown to produce cardiopulmonary changes similar to other α2-agonists, but of very short duration. Pharmacokinetic studies of dexmedetomidine in horses showed rapid distribution and rapid clearance. These pharmacokinetic characteristics favor its use as a CRI.\textsuperscript{26} The cost of the drug, however, still represents the major obstacle to the routine use of dexmedetomidine in equine sedation.

The intravenous solutions of α2-agonists for infusion for a 450-kg horse can be prepared by the following:

- 400 mg xylazine added to a 500-mL bag of saline (0.8 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.65 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.3 mg/kg/h)
- 20 mg romifidine added to a 500-mL bag of saline (0.04 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.03 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.015 mg/kg/h)
- 25 mg of detomidine added to a 500-mL bag of saline (0.05 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides
approximately 80 minutes of infusion at 0.04 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.02 mg/kg/h)

- 3.5 mg of dexmedetomidine added to a 500-mL bag of saline (0.007 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.005 mg/kg/h. When combined with opioids, the infusion rate should be decreased to 1 drop/2 s (0.002 mg/kg/h)

**α2-ANTAGONISTS**

The α2-antagonist atipamezole (0.05–0.15 mg/kg IM) has been used successfully to reverse sedation from detomidine, xylazine, romifidine, and medetomidine. Atipamezole completely reverses the sedation, but recurrence of sedation can occur if high doses of α2-agonist are used, mainly due to the short duration of action of atipamezole.27

**Opioids**

The analgesic effect of opiates in horses still represents a major topic of discussion and current investigation. The effect of opioids on somatic and visceral pain has been largely investigated in horses.28–32 Opioids have also been shown to provide a significant synergistic effect on sedation produced by α2-agonists. The combination of an α2-agonist with an opioid allows a significant reduction of the effective dose of either agent to about half of the dose of each drug used alone (see Table 4).33–36

The potential side effects of opioids have limited their widespread use in the past. Signs of excitement, such as head shaking and continuous pacing and gastrointestinal hypomotility, are the most feared adverse effects. These complications are rare at analgesic doses, but they can occur at much higher doses (0.5–1 mg/kg morphine) than those used clinically.37–39 However, the debate on the safety of these agents is still open. Morphine has been implicated in postanesthetic colic in one institution,40 although results from other studies showed no such risk.41,42 A reduction in fecal output has been reported in horses given morphine. However, general anesthesia, pain, stress, and changes in diet have all been shown to produce a significant effect on gastrointestinal motility.43–46 Fecal output is also easily monitored and adding oil to feed may be considered if there is any concern about gastrointestinal motility. The authors encourage the use of opioid analgesics in horses whenever invasive surgical procedures are performed, given that the benefits of their use largely outweigh the risks.47

Opioid-induced histamine release, causing urticaria and hypotension, is possible after rapid intravenous injection. This occurrence is particularly rare; however, opioids should be given by slow injection when administered intravenously. Histamine release is more commonly seen after meperidine administration, so this drug, if ever used in horses, should only be administered by the intramuscular route.48

Recommended bolus doses and infusion rates are listed below and reported in Table 2.

**Butorphanol**

A single intravenous bolus has a short duration of action, between 30 and 60 minutes. CRIs of butorphanol, used to maintain a steady level of sedation and decrease possible behavioral side effects, have been described.49 A loading dose of 0.02 mg/kg intravenously, followed by an infusion rate of 0.024 mg/kg/h, was shown to produce both sedative and analgesic effects, without causing behavioral changes, whereas a single dose of butorphanol (0.1 mg/kg, IV) resulted in a significant increase in locomotor activity and ataxia. The use of butorphanol has been associated with increased head
shaking and twitching, so it is not ideal for procedures requiring the head to be static (ie, ocular procedures). When combined with \(\alpha_2\)-agonists, butorphanol produces a potent synergistic effect. Individual CRI doses should be halved to avoid oversedation.\(^{35,50}\)

**Morphine and methadone**

Morphine at 0.1 to 0.2 mg/kg intravenously produces sedation and analgesia of longer duration than butorphanol. The effect after bolus administration lasts 4 to 6 hours. Morphine has been used successfully as an infusion at 0.03 mg/kg/h, following an initial bolus of 0.05 mg/kg intravenously, in combination with an \(\alpha_2\)-agonist for standing surgery.\(^{51}\) Methadone at 0.15 mg/kg intravenously produces a similar degree of sedation to morphine, but the rate for constant infusion has not been determined at present.\(^{37}\) The authors have used methadone as a CRI at 0.05 mg/kg/h combined with \(\alpha_2\)-agonists for standing sinus surgery with successful results.

**Buprenorphine**

Buprenorphine has recently been studied in horses and appears to provide satisfactory analgesia for 8 to 12 hours.\(^ {52,53}\) Buprenorphine at 0.005 to 0.01 mg/kg intravenously has been shown to provide adequate analgesia in combination with \(\alpha_2\)-agonists for standing laparoscopy.\(^ {54}\) The onset of analgesia is slow and the peak effect occurs at 45 to 60 minutes after bolus administration.\(^ {55,56}\) Given the long duration of action of buprenorphine, no constant infusion for this agent has been investigated.

The intravenous solutions of opioids for infusion for a 450-kg horse can be prepared by adding the following:

- 15 mg butorphanol to a 500-mL bag of saline (0.03 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.024 mg/kg/h. When combined with \(\alpha_2\)-agonists, the infusion rate should be decreased to 1 drop/2 s (0.012 mg/kg/h)
- 20 mg morphine to a 500-mL bag of saline (0.04 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.03 mg/kg/h. When combined with \(\alpha_2\)-agonists, the infusion rate should be decreased to 1 drop/2 s (0.015 mg/kg/h)
- 30 mg methadone to a 500-mL bag of saline (0.06 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.05 mg/kg/h. When combined with \(\alpha_2\)-agonists, the infusion rate should be decreased to 1 drop/2 s (0.025 mg/kg/h)

### Table 2

Recommended intravenous boluses and CRI for opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Intravenous Bolus and Infusion Rate</th>
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<tbody>
<tr>
<td>Butorphanol</td>
<td>Bolus: 0.02 mg/kg CRI: 0.024 mg/kg/h</td>
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<tr>
<td>Morphine</td>
<td>Bolus: 0.1–0.2 mg/kg CRI: 0.03 mg/kg/h</td>
</tr>
<tr>
<td>Methadone</td>
<td>Bolus: 0.15 mg/kg CRI: 0.05 mg/kg/h</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Bolus: 0.005–0.01 mg/kg</td>
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Ketamine

Ketamine, besides its common use as an induction agent, can be administered at sub-anesthetic doses in standing horses to provide analgesia, particularly in cases of inflammatory diseases. Ketamine is effective in cases whereby adjunctive analgesia is required. The duration of action of a subanesthetic ketamine bolus (0.1–0.5 mg/kg) is short (30 minutes). At these doses, ketamine appears to provide somatic analgesia and rapid onset of sedation. An infusion of ketamine may then be beneficial for a prolonged procedure when the analgesia provided by α2-agonists or opioids appears insufficient. Ketamine can be infused at 0.3 to 0.6 mg/kg/h intravenously, with minimal side effects (Table 3). Ketamine can be used in combination with α2-agonists, opioids, and/or lidocaine for extended infusion. When using combinations, the individual infusion rates should be maintained at the lower end of the dose range to avoid oversedation.

Ketamine is also useful in cases of insufficient sedation from α2-agonists. A bolus of 0.1 to 0.2 mg/kg intravenously is effective as rescue intervention in the case of intra-procedural sudden lightening of the level of sedation. A 50-mg (0.1 mg/kg) intravenous bolus in an average adult horse would provide rapid onset of profound sedation with the horse remaining still for about 15 minutes. This intervention, referred to as the “ketamine stun,” should only be used while the sedation from another agent is still effective to avoid excitation.

In recent years, ketamine has been shown to possess several properties beyond its anesthetic and analgesic activity. Most interestingly, ketamine has a substantial anti-inflammatory effect by down-regulating the production of pro-inflammatory cytokines. In virtue of this action, ketamine has been gaining interest for use in the course of laminitis and other severe inflammatory processes in horses.

The intravenous solutions of ketamine for infusion for a 450-kg horse can be prepared as follows:

- 200 mg ketamine added to a 500-mL bag of saline (0.4 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.3 mg/kg/h.

Lidocaine

Lidocaine can be administered systemically in horses to provide analgesia, sedation along with anti-inflammatory, prokinetic, and anti-endotoxaemic effects. The mechanisms whereby systemic lidocaine exerts analgesic and nonanalgesic actions have not been fully elucidated, but activity on specific peripheral and central sodium channels has been hypothesized. Following a loading dose of 1 to 2 mg/kg given intravenously over 5 to 10 minutes, lidocaine is usually infused at 0.025 to 0.05 mg/kg/min (see Table 3).

One important consideration when using lidocaine is the relatively low therapeutic index of this drug. Noticeably, the high end of the effective dose approximates closely

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Recommended intravenous boluses and CRI for ketamine and lidocaine</th>
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<tbody>
<tr>
<td>Drug</td>
<td>Recommended Intravenous Bolus and Infusion Rate</td>
</tr>
<tr>
<td>Ketamine</td>
<td>Bolus: 0.1–0.2 mg/kg CRI: 0.3–0.6 mg/kg/h</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Bolus: 1–2 mg/kg CRI: 0.025–0.05 mg/kg/min</td>
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the dose at which adverse effects may start to occur. The plasma concentration for central nervous system (CNS) side effects in horses is 2 to 3 times the target therapeutic level achieved using the rate of 50 μg/kg/min. Toxic plasma levels can therefore be easily achieved by accumulation of lidocaine with prolonged infusions. The first signs of toxicity are CNS effects, which can present as muscle fasciculations, anxiety, and incoordination. This can progress to loss of consciousness, seizures, and respiratory arrest if severe overdosing occurs. If muscle fasciculations are seen, then the rate should be halved or stopped. Because lidocaine is rapidly metabolized, cessation of therapy or reduction of infusion rate may be all that is required to relieve minor symptoms. Seizures or excitement should be treated with induction of general anesthesia rather than diazepam alone. This recommendation is based on the risk of worsening the incoordination and delirium by using diazepam alone.

If cardiovascular collapse occurs, it should be treated with aggressive fluid resuscitation and vasopressor agents. Rarely, collapse occurs before the onset of muscle fasciculations; this is because there is large variation between individuals. Cardiovascular effects usually occur at a much higher plasma concentration than the one causing CNS signs. Cardiovascular side effects include bradycardia, hypotension, ventricular arrhythmias, and cardiac arrest.

The accumulation of lidocaine and its metabolites during a prolonged infusion (>2 hours) would likely produce ataxia. As a preventive measure, even in the absence of signs of toxicity, after 2 hours of infusion at the high-dose rate (0.05 mg/kg/min), it is then recommended to halve the rate (0.025 mg/kg/min).

The intravenous solutions of lidocaine for infusion for a 450-kg horse can be prepared by adding the following:

- 2000 mg lidocaine to a 500-mL bag of saline (4 mg/mL), administered at a rate of 1 drop/s (10 drops/mL infusion set). This solution provides 80 minutes of infusion at approximately 0.05 mg/kg/h. The infusion rate should be halved after 2 hours of infusion.

**SEDATIVE COMBINATIONS**

When sedative combinations are used, possible chemical interactions between different agents mixed in the same solution can cause precipitation and affect drug stability. To avoid this possible occurrence and to better titrate the effect of each sedative or analgesic drug of the combination, the authors recommend using separate infusion bags for each drug. Infusion rates for sedative combinations commonly used for standing sedation are listed in Table 4.

**EPIDURAL ANESTHESIA/ANALGESIA**

Caudal or intercoccygeal epidural anesthesia and analgesia provide desensitization of the tail, anus, rectum, perineum, vulva, vagina, urethra, and bladder in conscious standing horses. Local anesthetics, α2-agonists, ketamine, and opioids have been administered by caudal epidural injection, providing long-lasting pain relief in standing horses. The aim is to produce sensory desensitization without losing the motor function of the hind limbs. Numerous drug combinations have been described. A local anesthetic agent combined with an α2-agonist or an opioid is commonly used.

Epidural α2-agonists provide a direct analgesic effect and a synergistic action with local anesthetics, prolonging their duration of action. Epidural ketamine produces analgesia by a noncompetitive antagonist effect on spinal N-methyl-D-aspartate
receptors. Analgesia following epidural injection of opioids is mainly due to the local action on opioid receptors in the spinal cord. \(^{79,80}\) Epidural morphine, by virtue of its hydrophilic nature, produces profound analgesia with no detectable drug in the plasma. \(^{81}\) Lipid solubility of opioids injected epidurally affects the onset and duration of analgesia. Onset of analgesia is slower but the duration of analgesia is longer with hydrophilic agents such as morphine. \(^{79}\) Interestingly, highly lipophilic opioids, such as methadone, hydromorphone, and fentanyl, produce analgesia primarily by systemic absorption; hence, no advantage exists in injecting these agents epidurally. \(^{79}\)

The volume of anesthetic/analgesic injected epidurally depends on the size of the horse and type of agent used. If local anesthetics are used, no more than a total volume of 10 mL per adult horse should be injected, to avoid hind limb paralysis. \(^{82}\) Opioids, ketamine, and \(\alpha\)-agonists can be administered epidurally in adult horses, as diluted solution, at total volumes up to 20 mL. The commercially available solutions of these agents are usually highly concentrated and can be diluted with sterile saline to obtain the desired volume to be injected. A total volume of 20 mL per adult horse produces cranial migration of the solution for up to 10 vertebral spaces. \(^{56}\)

For single epidural injections, the authors recommend the use of an 18-G 7.5-cm spinal needle placed in the first intercoccygeal space (Co1-Co2) in standing horses held in stocks. Epidural catheterization is performed using an epidural Huber point (Tuohy) needle instead of a spinal needle. For a detailed description of the techniques for epidural injection and catheterization in horses, the reader is referred to a recent review article on the topic. \(^{83}\)

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Recommended intravenous CRI for common sedative combinations (See the text for details on how to prepare infusion bags of each agent of the sedative combination. The solutions for infusion of each sedative or analgesic drug should be prepared in separate bags. It is not recommended to mix multiple drugs in the same infusion bag, due to the risk of possible chemical interactions.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Combinations</td>
<td>Recommended Intravenous Infusion Rate</td>
</tr>
<tr>
<td>Detomidine</td>
<td>0.02 mg/kg/h</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.012 mg/kg/h</td>
</tr>
<tr>
<td>Xylazine</td>
<td>0.03 mg/kg/h</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.012 mg/kg/h</td>
</tr>
<tr>
<td>Romifidine</td>
<td>0.015 mg/kg/h</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.012 mg/kg/h</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>0.002 mg/kg/h</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.012 mg/kg/h</td>
</tr>
<tr>
<td>Detomidine</td>
<td>0.02 mg/kg/h</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.015 mg/kg/h</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>0.002 mg/kg/h</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.015 mg/kg/h</td>
</tr>
<tr>
<td>Detomidine</td>
<td>0.02 mg/kg/h</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.015 mg/kg/h</td>
</tr>
<tr>
<td>Ketamine</td>
<td>0.3 mg/kg/h</td>
</tr>
<tr>
<td>Xylazine</td>
<td>0.03 mg/kg/h</td>
</tr>
<tr>
<td>Ketamine</td>
<td>0.3 mg/kg/h</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>0.025 mg/kg/h</td>
</tr>
</tbody>
</table>
Epidural catheterization can be used for repeated epidural delivery of analgesics and anesthetics in horses (Fig. 1). Continuous epidural drug administration in horses has been repeatedly shown to produce profound analgesia in various clinical conditions. Long-term epidural drug administration is not associated with apparent adverse

![Epidural catheter inserted between first and second coccygeal vertebrae for long-term use. The catheter must be secured to the skin using a tape butterfly sutured to the skin. A bacterial filter may be attached to the catheter connector. The site of catheter penetration should be maintained sterile and the region should be covered with sterile gauze sponges and an adhesive plastic dressing.](image)

**Table 5**
Common single agents and drug combinations for epidural analgesia/anesthesia in standing adult horses (if local anesthetic is used, no more than a total volume of 10 mL per adult horse is injected. Opioids, ketamine, and α2-agonists can be administered epidurally in adult horses, as diluted solution at total volumes up to 20 mL. The commercial solutions of these agents are usually highly concentrated and can be diluted with sterile saline to obtain the desired volume to be injected.)

<table>
<thead>
<tr>
<th>Recommended Agents for Epidural Use</th>
<th>Recommended Volume of Solution per Adult Horse (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Local anesthetics</strong></td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2%</td>
<td>5</td>
</tr>
<tr>
<td>Mepivacaine 2%</td>
<td>5</td>
</tr>
<tr>
<td>Bupivacaine 0.25%</td>
<td>10</td>
</tr>
<tr>
<td>Ropivacaine 0.2%</td>
<td>10</td>
</tr>
<tr>
<td><strong>α2-agonists</strong></td>
<td></td>
</tr>
<tr>
<td>Xylazine (0.17 mg/kg)</td>
<td>10</td>
</tr>
<tr>
<td>Detomidine (0.02 mg/kg)</td>
<td>10</td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
</tr>
<tr>
<td>Morphine (0.1 mg/kg)</td>
<td>20</td>
</tr>
<tr>
<td><strong>Other agents</strong></td>
<td></td>
</tr>
<tr>
<td>Ketamine (1 mg/kg)</td>
<td>20</td>
</tr>
<tr>
<td><strong>Drug combinations</strong></td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2% + Xylazine (0.17 mg/kg)</td>
<td>5–8</td>
</tr>
<tr>
<td>Lidocaine 2% + Morphine (0.1 mg/kg)</td>
<td>5–8</td>
</tr>
<tr>
<td>Xylazine (0.17 mg/kg) + Morphine (0.1 mg/kg)</td>
<td>20</td>
</tr>
<tr>
<td>Bupivacaine 0.25% + Morphine (0.1 mg/kg)</td>
<td>10</td>
</tr>
<tr>
<td>Detomidine (0.02 mg/kg) + Morphine (0.1 mg/kg)</td>
<td>20</td>
</tr>
</tbody>
</table>
systemic effects in horses. Minor complications associated with epidural catheters are mainly related to catheter malfunction rather than to injury to the patient.69,84,85

Single agents and drug combinations for epidural injection, with relative dosages and volume of injection in adult horses, are shown in Table 5.

REFERENCES


