How to Provide Pain Relief for Laminitis in the Field

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1. Introduction
Laminitis is an extremely painful condition with still incompletely understood pathophysiology.1–3 All too often, the uncontrollable severe pain associated with the disease is the single most common reason for euthanasia of laminitic horses. Treatment is frequently unfinished because owners and health providers feel forced to end the extreme pain and suffering by ending the life of the afflicted animal. More positive treatment results could be obtained if pain and suffering could be successfully modulated.4 Non-steroidal anti-inflammatory drugs (NSAIDs) such as flunixin meglumine and phenylbutazone have long been and still remain the primary pharmacologic agents used to treat pain and inflammation in horses with laminitis.5

Tramadol is emerging as an additional option toward providing multimodal analgesia in equine laminitis,6 and its efficacy has been well established in neuropathic and inflammatory pain states.7–10 Because it is now known that pain associated with laminitis has both inflammatory and neuropathic components,11,12 targeted multimodal analgesic therapies probably will be necessary for effective pain modulation. Drugs such as ketamine and gabapentin may be very beneficial in modulating neuropathic pain as well as pathologic pain states characterized by hyperalgesia (ie, exaggerated response to a painful stimulus) and allodynia (ie, pain response to a normally nonpainful stimulus).6,13–15

The goal of this report is to present techniques targeting such pathologic pain states that can be used to manage pain and suffering in horses with laminitis.

2. Recommended Agents and Routes of Administration
Tramadol tablets can be crushed into powder, mixed with syrup or molasses, and administered orally at a dose of 5 mg/kg q 12 hours.6

Ketamine can be administered intravenously as a constant rate infusion at a dose of 0.6 mg/kg per hour for 6 hours/day for 3 to 5 days (or longer as needed) through a syringe pump,6 or it can be diluted in 0.9% saline and dripped by gravity. Alternatively, it can be administered intramuscularly at 0.5 mg/kg q 6 hours.14

Gabapentin can be administered orally at doses ranging from 2.5 to 20 mg/kg q 8 hours, q 12 hours, or q 24 hours, as needed.13–15

3. Evidence of Efficacy
When administered alone, tramadol was shown to produce significant initial improvement (3 of 7 days)
in off-loading frequency in analgesic-naive horses with pain caused by chronic laminitis. In this same study, ketamine administered intravenously for the first 3 days of treatment significantly improved off-loading frequency and forelimb load during (7 of 7 days) and after (3 days) tramadol therapy. Tramadol and ketamine had a modulatory role in the plasma levels of the pro-inflammatory cytokine tumor necrosis factor-α and the vasoconstrictor prostanoid thromboxane-A₂. Gabapentin has been used as part of a multimodal analgesic protocol and was shown to help in the pain management of two horses with presumptive diagnosis of neuropathic pain.  

4. Discussion

Laminitis pain is associated with increased off-loading frequency, decreased forelimb load, and other behavioral and cellular changes congruent with pathologic pain states characterized by hyperalgesia and allodynia. Pain relief with tramadol results from complex interactions with opioid, adrenergic, and serotonin receptor systems and possibly through modulation of inflammatory mediators such as pro-inflammatory cytokines and prostanoids. In analgesic-naive horses with chronic laminitis, co-administration of tramadol and ketamine resulted in significant improvement in off-loading frequency, forelimb load, and plasma levels of a major pro-inflammatory cytokine and a critical vasoconstrictor prostanoid. It is possible that co-administration of tramadol with NSAIDs could result in greater modulation of inflammatory responses and superior pain management than when each drug is used alone.

Ischemia and inflammation in the early stages of laminitis probably cause neuronal injury that eventually shifts the acute inflammatory pain into a chronic syndrome with a prominent neuropathic component. The precise timing and nature of these events are not precisely known, but it may be established in as early as a few days. The neuropathic pain component in laminitic horses is not well responsive to NSAIDs and opioids but typically responds to modulators of N-methyl-D-aspartate receptors (ie, ketamine) and voltage-gated calcium channels (gabapentin) in nociceptive neurons in the spinal cord and brain. The beneficial effects of these drugs have been demonstrated in horses with apparent neuropathic pain. The equine practitioner should consider introducing these therapeutic modalities as soon as it is perceived that the current standard of care is not producing the desired pain control. The use of NSAIDs, tramadol, ketamine, and/or gabapentin appears to be a sound mechanistic-based approach in providing multimodal pain management in horses with laminitis.

References