Intravenous lidocaine has potential uses for adjunctive treatment of pain, ileus, and endotoxemia in horses. Although human clinical literature and experimental studies suggest that lidocaine may be effective for these conditions, the equine literature is limited and conflicting. A review of the mechanisms of action, pharmacokinetic studies, and clinical uses of lidocaine in horses is presented. Author’s address: The Ohio State University, Veterinary Teaching Hospital, 601 Vernon Tharp Street, Columbus, OH 43210; e-mail: mudge.3@osu.edu. © 2007 AAEP.

1. Introduction
The use of IV lidocaine in horses has gained popularity for the treatment of post-operative ileus (POI), the management of pain, and the adjunctive treatment of sepsis and endotoxemia. Lidocaine has gained wide acceptance as a local anesthetic and anti-arrhythmic agent, and it is the most commonly administered prokinetic drug for POI in horses. Lidocaine and other local anesthetics have been studied extensively to determine their potential antinociceptive and anti-inflammatory effects. Experimental and clinical studies have given us rationale for extending the use of IV lidocaine to cases of pain, POI, and sepsis; however, the clinical utility of IV lidocaine in horses remains controversial. A review of the pharmacology of lidocaine and the experimental and clinical evidence of its effects in horses and humans may help to clarify the role of lidocaine in clinical equine practice.

2. Pharmacology and Pharmacokinetics of Lidocaine
Lidocaine hydrochloride is an amide local anesthetic and is also classified as a class IB anti-arrhythmic agent. The mechanism of action is believed to be through blockage of the sodium channel. The onset of action is rapid when administered intravenously (within 2 min), and the terminal half-life in awake horses has been reported as 79 ± 41 min. The therapeutic range is considered to be 1–5 µg/ml, and toxic effects have been reported at ranges of 1.9–4.5 µg/ml. The most common adverse effects of lidocaine include depression, ataxia, and muscle tremors, and these effects usually resolve rapidly after the lidocaine infusion is discontinued. At higher levels (overdose), hypotension, bradycardia, and seizures have been reported.

The most commonly reported dosage of lidocaine for use as an infusion in post-operative horses is a loading dose of 1.3 mg/kg by IV bolus followed by a constant rate infusion of 0.05 mg/kg/min. In awake horses with or without gastrointestinal disease, this dosing regime results in plasma concentrations of 1–2 µg/ml. Long-term infusions may result in higher plasma concentrations, especially when used in combination with highly protein-bound drugs such as flunixin or ceftiofur. Serum lidocaine concentrations have also been reported to be higher in anesthetized horses.
3. Use of Lidocaine for Analgesia

Lidocaine is commonly used as a local anesthetic, but it has received recent attention for its potential analgesic effects when absorbed or administered systemically. The proposed mechanism of analgesic or antinociceptive effect includes blockade of the sodium channels or potassium currents in the dorsal horn of the spinal cord. The antinociceptive action may also be specifically related to the inhibition of aberrant electrical discharges from injured peripheral nerves.

The use of local anesthetics for relief of neuropathic pain in humans gives some veterinarians insight into possible analgesic applications of lidocaine. A systematic review of systemically administered local anesthetics for relief of neuropathic pain revealed a therapeutic benefit similar to morphine and gabapentin and superior to placebo for a variety of conditions.

In horses, lidocaine infusions have been used as an adjunct to anesthesia, and they have been shown to decrease halothane mean alveolar concentration in a dose-dependent fashion. A study of the electroencephalographic changes during castration of ponies under halothane anesthesia also showed an antinociceptive effect from lidocaine. An experimental model of visceral and somatic nociception in conscious horses showed that lidocaine may play a role in somatic analgesia, but it failed to show an effect on visceral nociception (rectal-balloon model). The use of lidocaine as an adjunct to pain management in post-operative large-colon volvulus cases has been reported, and I have used lidocaine for the management of gastrointestinal, musculoskeletal, and other soft tissue pain with subjective improvement in many cases.

4. Use of Lidocaine for Gastrointestinal Ileus

Intravenous lidocaine has been used in humans to prevent post-operative pain and ileus after radical retropubic prostatectomy. Earlier return to bowel function and pain relief were also attributed to the use of lidocaine in patients undergoing colonic surgery, which is a patient population that is particularly at risk of POI. Lidocaine-treated patients had significantly faster returns to bowel function, decreased pain, and shorter hospital stays.

In horses, abnormal motility occurs commonly in cases of ileus after small-intestinal surgery and in cases of proximal duodenitis-jejunitis. Several retrospective and prospective studies suggest that lidocaine may have a role in preventing the development of POI or in speeding the resolution of POI in horses. A study of horses with POI or enteritis showed a faster return to bowel function and shorter hospitalization times in lidocaine-treated horses. Experimental in vitro studies show that lidocaine increases motility in the proximal duodenum of horses. The prokinetic mechanism of action is unclear and is likely to be complex. Possible mechanisms include a direct stimulation of motility, a decrease in sympathetic tone, an inhibition of neuropehormonal factors, and an inhibition of abnormal motility patterns. The anti-inflammatory, anti-endotoxic, and analgesic effects of lidocaine may also contribute to resolution of ileus in injured bowels.

There is conflicting experimental evidence that lidocaine may, in fact, decrease intestinal motility in horses. A recent study of the effect of lidocaine on the jejunal motility of normal horses showed a decrease in motility for the lidocaine-treated horses. This study, along with clinical reports that suggest limited efficacy of lidocaine and other prokinetics for the treatment of POI, raises the question of whether or not we should be using lidocaine for the treatment of horses with POI or proximal enteritis-jejunitis. We do not currently have enough evidence to determine which cases may respond to lidocaine infusion for the treatment of POI, nor do we have enough information to determine whether there is a dose-dependent effect of lidocaine on the gastrointestinal tract. It is possible that lidocaine suppresses abnormal motility in injured bowels while having no effect or negative effect on motility in normal bowel.

The potential effects of lidocaine on bowel inflammation, edema, and reperfusion injury also suggest that lidocaine may be useful as a prokinetic for injured bowel but not for healthy bowel.

5. Use of Lidocaine for Sepsis

There are numerous animal model studies that show an anti-inflammatory and anti-endotoxic effect of systemically administered lidocaine. The proposed mechanisms of action include inhibition of polymorphonuclear granulocyte response, migration, adhesion, and free-radical release. Inhibition of the acute cytokine response and macromolecular leakage may also help to prevent endothelial and end-organ damage in severe sepsis.

An in vivo study performed in horses showed a significant treatment effect of lidocaine in reducing mucosal damage in horses with intestinal ischemia-reperfusion injury. Based on the proposed mechanisms of action, lidocaine may have a role in the treatment of ischemia-reperfusion injury in cases of small-intestinal and large-colonic strangulation. Additionally, a model of laminitis shows the role of leukocyte emigration in the development of laminitis, and it is possible that local anesthetics such as lidocaine could attenuate the leukocyte responses.

The inhibitory effects of lidocaine on leukocyte response have raised the question of an increased susceptibility to infection in lidocaine-treated animals. There does not seem to be an increased incidence of peritonitis or incisional infection in post-operative colic patients treated with lidocaine; however, lidocaine may be contraindicated in cases with known contamination or bacterial infection.

6. Using IV Lidocaine in Practice

The use of local anesthetics as adjuncts in the treatment of pain, ileus, and endotoxemia is an exciting
topic with numerous potential clinical applications. The available studies in horses have given us valuable information about the pharmacokinetics and potential toxic effects of lidocaine. Although clinical studies suggest that lidocaine may be useful in the treatment of POI and somatic pain in horses, further work is needed to determine which horses may respond best to lidocaine and which doses of lidocaine may be most useful for various applications.

The dosage that I currently use for post-operative enteritis, ileus, and gastrointestinal pain is a slow bolus (1.5 mg/kg, IV) of 2% lidocaine that is followed by a constant-rate infusion (0.05 mg/kg/h). Because of the narrow therapeutic range of lidocaine, regulation of the infusion using fluid pumps or syringe pumps is recommended. The dose of 2% lidocaine can be injected into an empty, sterile 1-l bag for ease of administration. Alternatively, lidocaine can be placed in larger bags of IV fluids and administered by gravity flow, although regulation of the infusion is more difficult with this method.

Although the reported side effects of lidocaine in horses are usually dose dependent and usually resolve with discontinuation of the medication, caution is warranted because of the narrow therapeutic index of lidocaine. Muscle fasciculation and collapse have been reported in horses with lidocaine-plasma concentrations within the therapeutic range. I do not routinely monitor plasma-lidocaine concentrations in clinical cases; however, careful monitoring for muscle tremors, ataxia, and changes in mentation is performed, and the infusion is decreased or discontinued if adverse effects are noted.

When lidocaine is administered as an adjunct to general anesthesia, special caution may be warranted because of the risks of ataxia during recovery. Adverse effects in recovery from general anesthesia have not been reported in all studies, but a recent study found a significantly higher degree of ataxia and a tendency toward lower quality of recovery in lidocaine-treated horses. Valverde et al. recommended that the lidocaine infusion be discontinued 30 min before the end of surgery to help avoid complications with recovery.

In summary, IV lidocaine may be a useful adjunct to the treatment of gastrointestinal and surgical pain, ileus, and ischemia, although the infusion must be monitored closely to help avoid toxic effects. The mechanism of action of lidocaine, particularly as it relates to POI, requires further investigation to determine when the use of lidocaine is indicated. Clinical evaluation of lidocaine as an analgesic for other soft tissue and musculoskeletal conditions is also needed.

References and Footnotes


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