The Use of Lidocaine Patches

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ABSTRACT: Our recent pharmacokinetic studies with lidocaine patches in dogs and cats have found that plasma concentration of lidocaine following patch application tends to be low. Lidocaine patch application can be a powerful analgesic adjunct to existing analgesic agents, including opioids and NSAIDs, in a multimodal pain management scheme. This article reviews the pros and cons of lidocaine patch application and its clinical use in dogs and cats. A comparison of lidocaine and fentanyl patches is included.

Lidocaine, a local anesthetic of the amide class, has been used for many years by veterinarians in a variety of species and can be considered one of the most versatile local anesthetics because of its rapid onset of action and moderate duration of effect. Lidocaine can be administered intravenously, by infiltration, or topically. Topical application of various concentrations (0.5% to 4%) of lidocaine has been shown to have analgesic effects. In animals, topical application of local anesthetics has frequently been limited to ocular preparations because of the difficulty in penetrating animal skin with topical application alone. Lidocaine has been used in a eutectic mixture with other local anesthetics (2.5% lidocaine and 2.5% prilocaine [EMLA cream, AstraZeneca]) to improve penetration of the drug when it is applied to unbroken skin.

The lidocaine patch (Lidoderm, Endo Pharmaceuticals) is a topical analgesic transdermal patch that was approved for use in 1999 to treat human neuropathic pain induced by herpes zoster (shingles). According to the manufacturer of Lidoderm, the important difference between EMLA cream and the lidocaine patch is that EMLA cream is formulated with the intent to produce a local anesthetic effect by delivering sufficient lidocaine to block large, myelinated sensory fibers. Although this is very beneficial in treating acute pain, it may be a disadvantage in patients with neuropathic pain that may already have sensory loss in the affected areas.

The use of the lidocaine patch has generated interest in veterinary as well as human pain management. This article describes our experience of using lidocaine patches in dogs and cats.

PHYSICAL DESCRIPTION

Lidoderm is made from an adhesive material that contains 5% lidocaine. It is applied to a nonwoven polyester felt backing and covered with a polyethylene terephthalate film release liner. The release liner must be removed before the patch is applied to the skin. The lidocaine patch is self-adhesive following removal of the liner. The patch (Figure 1) is 10 by 14 cm and contains 700 mg of lidocaine (50 mg of lidocaine per gram of adhesive patch) in an aqueous base with other inactive ingredients. The patch is clean but nonsterile. Each carton comes with 30 patches at a cost of $4.50 to $6.00 per patch.
Lidocaine is not a controlled substance, but a prescription is needed to obtain the patch.

To date, another lidocaine patch is being developed commercially, and the manufacturer is seeking FDA approval for its use on humans. The patch is called LidoPAIN SP (EpiCept Corporation, Englewood Cliffs, NJ; SP represents surgical pain). The main difference between Lidoderm and LidoPAIN SP is that LidoPAIN SP is sterile and Lidoderm is not. Furthermore, LidoPAIN SP contains 10% lidocaine instead of the 5% in Lidoderm. The manufacturer is seeking approval of the patch for use in surgical procedures, including hernia repair, plastic surgery, puncture wound repair, biopsy, cardiac catheterization, and tumor removal.

**MECHANISMS OF ACTION**

The proposed mechanism of the lidocaine patch is that it allows the topically applied lidocaine to bind to neuronal membrane receptors and stabilize neuronal membranes by inhibiting sodium ion influxes, thereby inhibiting initiation of the action potential and conduction of nerve impulses. This prevents or reduces pain signal initiation and transmission from peripheral nerve axons to the central nervous system, thereby decreasing pain perception.

Human studies have shown that up to 5% (35 mg) of the lidocaine patch is absorbed topically, producing analgesia in 30 minutes, with a drug half-life of 6 to 8 hours. The dermally absorbed lidocaine appears to have a very low rate of systemic absorption, with a plasma level of approximately 0.13 µg/ml, resulting in local analgesia and not anesthesia. This is an interesting contrast to the analgesic effects of a regional lidocaine infiltration block. Humans do not report numbness or loss of sensitivity to touch, pressure, or temperature after lidocaine patch application. The exact mechanism of this differential effect is unknown. However, it has been suggested that the lidocaine patch delivers adequate amounts of lidocaine to block sodium channels on small injured or dysfunctional pain fibers, but not enough to block sodium channels on large, myelinated A-β sensory fibers. Therefore, the patch produces analgesia without blocking all the sensory and motor inputs. In humans, a lidocaine patch applied over a painful area on a limb actually improves motor function because of pain reduction and does not interfere with ambulation. Our clinical experience indicates that this may also be the case in dogs and cats.

In humans, the patch is said to treat three types of neuropathic pain induced by shingles:

- Constant, deep, aching or burning pain
- Intermittent, lancinating pain
- Allodynia (pain provoked by normally innocuous stimuli; e.g., light touch, heat, cold) that lasts well beyond the duration of the stimulus (hyperpathia)

It seems that lidocaine patches have multiple applications in treating dermal pain via a local analgesic mechanism.

Another recent study in humans with moderate-to-severe osteoarthritis of the knee reported a significant reduction in pain intensity after 2 weeks of treatment with a 5% lidocaine patch. The proposed mechanism of the lidocaine patch in alleviating joint osteoarthritis pain is that primary afferent neurons located in affected joints express excessive amounts of abnormally functioning sodium channels on their surface in response to the inflammatory process. These sodium channels may play an essential role in producing pain and hyperalgesia, and topical application of a lidocaine patch can suppress pain signals via local inhibition of sodium channels.

Preliminary studies of the LidoPAIN SP patch have shown that humans who received it following hernia surgery had increased relief of postsurgical incisional pain and required fewer doses of NSAIDs and patient-controlled, systemically delivered opioids. The sterile patches were applied directly over the incision after closure and left for 72 hours. Lidocaine patches can likely be a vital part of soft tissue pain management.

**PHARMACOKINETICS**

A human study showed that following intravenous lidocaine administration, plasma lidocaine concentrations reaching 1.5 µg/ml (1,500 ng/ml) significantly reduced neuropathic pain. A neuropathic pain model using rats showed that a plasma lidocaine concentration...
A recent study reported the plasma levels (110 and 90 ng/ml) were 103.55 and 140 ng/ml, respectively, in dogs. Our study demonstrated that evaluating a greater area of exposure to lidocaine patches in dogs resulted in rapid uptake (by 0.37 ± 0.26 hours; range: 0.11 to 0.81 hours) of lidocaine and reached a peak concentration of 1,450 ± 360 ng/ml (range: 800 to 1,860 ng/ml). No systemic toxic effects were observed, but skin irritation (redness) was evident on some dogs; this was not considered clinically significant. The plasma concentrations were considered to be very low but higher than those reported by Weiland et al with only one patch on each dog.

Key Points

• The lidocaine patch is generally safe to use on dogs and cats when applied for 3 to 5 days for pain management.
• Plasma lidocaine concentrations following patch application remain low and reach a steady state after 12 to 60 hours in dogs and cats.
• Minimal clinical side effects were associated with lidocaine patch application on dogs and cats.
• The lidocaine patch is not a controlled substance and can provide a long duration of action as an analgesic adjunct.
• In the near future, the lidocaine patch will likely play an important role in multimodal pain management in dogs and cats.

of 0.5 µg/ml (500 ng/ml) is required to achieve analgesia. In humans, the amount of drug absorbed is directly proportional to the skin surface area covered and the duration of patch application. A recent study investigated the pharmacokinetics of the lidocaine patch in dogs. A patch was applied for 12 hours to dogs weighing 20.7 to 31.7 lb (9.4 to 14.4 kg). It was applied to the skin of the lateral thorax where hair had been clipped or removed by depilation. Peak plasma lidocaine concentrations were obtained after 10 hours in the clipped hair group (62.94 ng/ml) and after 9 hours in the depilatory group (103.55 ng/ml). Patches were applied for 60 hours in a second experiment. The mean peak lidocaine plasma concentration was 45 ng/ml after 24 hours, with a final concentration of 29.37 ng/ml after 60 hours. This study suggests that there is minimal absorption of lidocaine from the patch in dogs. All dogs tolerated the patch well, with little of the redness or irritation reported in people.

We (JK, AW, and colleagues) conducted a similar study that evaluated a greater area of exposure to lidocaine patches in dogs. Seven dogs weighing 41.6 to 44 lb (mean: 44.9 ± 3 lb; 18.9 to 20 kg [mean: 20.4 ± 1.37 kg]) were used. The hair on the ventral abdominal midline was clipped and the skin cleaned with alcohol. Two 10-by-14-cm, 5% lidocaine patches were placed, with one on each side of the ventral abdominal midline, for 72 hours. A plasma concentration (60 ng/ml) of lidocaine was not detected until 12 hours after patch application, and the peak level was obtained after 36 hours (140 ng/ml). However, this delay in detecting a plasma lidocaine concentration is likely due to the limitation of the minimal detectable lidocaine concentration assay used in our study (limited to 50 ng/ml). Weiland et al. reported a mean absorption half-life within 2 hours when using 0.8 ng/ml as the minimal detectable lidocaine concentration. In our study, the plasma levels (110 and 90 ng/ml) were maintained at 48 and 60 hours, respectively. The patches were removed after 72 hours, and the plasma lidocaine level remained detectable 78 hours after application. It became undetectable by 82 hours.

No systemic toxic effects were noticed, but skin irritation (redness) was evident on some dogs; this was not considered clinically significant. The plasma concentrations were considered to be very low but higher than those reported by Weiland et al with only one patch on each dog.

ADVERSE REACTIONS

In humans, several types of adverse reactions (e.g., local, allergic, systemic) to the lidocaine patch have been reported. Reports of local reactions include erythema, hives, and edema due to patch application. These reactions were mild and transient, resolving spontaneously within a few minutes to hours after patch removal. Local skin irritation following patch application was not observed in one canine study. In our study involving application of two patches on the ventral midline, a small number of dogs (two of seven) had skin redness at the site of patch application, but it was transient and not clinically significant. We have not seen erythema, hives, or edema in our clinical cases in either dogs or cats.

Systemic lidocaine toxicosis from a lidocaine patch is unlikely in humans because of low absorption through the skin. A similar conclusion has been made for dogs. Systemic administration of 8 mg/kg of lidocaine with epinephrine (1:400,000) intraperitoneally, together with infiltration of 2 mg/kg of lidocaine with epinephrine (1:200,000) on the abdominal incision in dogs, resulted in rapid uptake (by 0.37 ± 0.26 hours; range: 0.11 to 0.81 hours) of lidocaine and reached a peak concentration of 1,450 ± 360 ng/ml (range: 800 to 1,860 ng/ml). No signs of toxicosis were observed in these experimental dogs in the follow-up study 18 hours after administration. Another study demonstrated that lidocaine had a myocardial depressant effect (systolic shortening) at plasma concentrations greater than 1,000 ng/ml when lidocaine was directly infused into the coronary arteries of dogs. The reported peak plasma concentrations of lidocaine in dogs with patches in a published study were 103.55 and 140 ng/ml, respectively, which are 10-fold lower than concentrations reported in other studies.
In our clinical experience, cats with lidocaine patches react similarly to dogs. Although cats are reportedly more susceptible to lidocaine toxicosis than are dogs, we have not seen cats with adverse reactions when appropriately sized patches are applied. In addition, a recent pilot study has shown that lidocaine patch application on cats results in a low plasma lidocaine concentration similar to that in dogs. An intact 5% lidocaine patch applied to the thorax of cats resulted in only one-tenth of the peak lidocaine concentration achieved from a 2-mg/kg IV lidocaine bolus. In contrast, the lidocaine concentration in the skin and muscle beneath the patch was 100-fold higher than the peak plasma lidocaine concentration in the same cat.

When we collectively compared systemic and local skin concentration 72 hours after lidocaine patch application in cats, we found a mean plasma lidocaine concentration of 0.087 µg/ml and a mean skin concentration of 211 µg/ml under the patch. Therefore, there was a 2,425-fold difference between the skin and plasma concentrations. This strongly suggests that the lidocaine patch acts directly through local tissue penetration into the nerves instead of systemically.

Unlike in humans, one challenge of using lidocaine patches on dogs and cats is the possibility of oral ingestion following application. We saw an adult beagle that had ingested a whole lidocaine patch. Fortunately, no adverse signs were noted, and the patch passed out with stool the next day. Until further studies prove that ingestion of a lidocaine patch is safe, caution should be taken to prevent toxicosis. Potential systemic signs of lidocaine overdose include toxic cardiovascular effects, such as bradycardia, hypotension, and eventually cardiac arrest. Other early signs of toxicosis include muscle or facial twitching, tremors, and seizures. If toxicosis occurs, lidocaine patches should be immediately removed and supportive therapy provided, including careful monitoring, fluid therapy, and inotropic therapy, if necessary, to improve cardiac performance. The use of lidocaine patches on cats warrants further investigation of plasma lidocaine levels in this species.

SIMILARITIES AND DIFFERENCES BETWEEN FENTANYL AND LIDOCAINE PATCHES

In veterinary medicine, the use of fentanyl patches has gained widespread acceptance in pain management, making drug administration via the transdermal route very popular. The similarities and differences between fentanyl and lidocaine patches follow:

- Because systemic absorption of lidocaine from the patch is low, lidocaine patches have potentially less severe systemic side effects than fentanyl patches, which have a different mechanism of action. Lidocaine patches act locally through topical absorption, and systemic concentrations of lidocaine are low. Fentanyl patches deliver the drug transdermally for systemic absorption. The greater the systemic absorption of fentanyl from the patch, the greater the systemic
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side effects and potential interactions with other drugs. However, it could be argued that a large lidocaine overdose can be lethal, whereas toxicosis associated with fentanyl may be treated, if detected early.

- In humans, lidocaine patches reportedly have a shorter onset (approximately 30 minutes) of pain relief than fentanyl patches (at least 12 to 24 hours). In dogs, however, peak plasma lidocaine concentrations have reportedly been reached in 10 to 24 hours via transdermal patches.

- Lidocaine patches must be applied close to the site of pain to function locally, whereas fentanyl patches can be applied anywhere on the skin for systemic uptake.

- Unlike fentanyl patches, lidocaine patches may be cut to fit the size of the patient or site of application without affecting the drug delivery system. Cutting fentanyl patches disrupts the delivery system, resulting in increased and uncontrolled delivery of the drug. Some clinicians advocate folding back the adhesive of the fentanyl patch for use on small patients such as cats.

- Lidocaine patches provide a physical barrier to prevent external mechanical stimulation of the painful site.

- Unlike fentanyl, lidocaine is not a controlled drug. However, both lidocaine and fentanyl patches require a prescription.

- Lidocaine patches may be less expensive than fentanyl patches.

- Unused, cut portions of lidocaine patches can be stored and used on other patients.

- Lidocaine patches have a duration of effect of 3 days or longer.

- We suspect that lidocaine patches are less likely to be affected by skin and body temperature than fentanyl patches because lidocaine patches appear to be less reliant on skin absorption to achieve therapeutic plasma concentrations for clinical effect. Further exploration of the effect of temperature on drug release and skin absorption is needed.

**Table 1. Lidocaine Patches (10 × 14 cm): Dosing Guideline for Dogs and Cats**

<table>
<thead>
<tr>
<th>Body Weight (lb; kg)</th>
<th>Patch(es)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–5; 1.4–2.3</td>
<td>One-sixth to one-quarter</td>
</tr>
<tr>
<td>6–10; 2.7–4.5</td>
<td>One-half</td>
</tr>
<tr>
<td>11–20; 5–9.1</td>
<td>One</td>
</tr>
<tr>
<td>21–40; 9.5–18.2</td>
<td>Two</td>
</tr>
<tr>
<td>41–60; 18.6–27.3</td>
<td>Two and one-half to three</td>
</tr>
<tr>
<td>61–100; 27.7–45.5</td>
<td>Three to four</td>
</tr>
</tbody>
</table>

**CLINICAL APPLICATION**

We have applied lidocaine patches to dogs and cats that have undergone elective and regular surgeries. Patients that
have undergone abdominal surgery, including ovariohysterectomy or laparotomy, can benefit from lidocaine patch application at the ventral abdominal midline. The patch can also be applied after thoracotomy, sternotomy, dorsal hemilaminectomy, cruciate repair, total ear canal ablation, and amputations.

For surgical cases, lidocaine patches should be applied at the end of the surgery after skin closure. Because the currently available lidocaine patch is non-sterile, a nonadherent sterile pad or gauze (Telfa, The Kendall Company, Mansfield, MA) should be applied directly over the surgical wound before patch application. Before application, the lidocaine patch should be cut to the length of the surgical incision and the protective back liner removed. The lidocaine patch is self-adhesive. After the skin has been closed and the area of application cleaned, cut patches should be applied on each side of the incision (Figure 2) to alleviate skin and muscle pain following surgery. A surgical film (Hypafix, Smith & Nephew, Auckland, NZ) can be used to cover the entire area (Figure 3), including the lidocaine patch and nonadhesive pad. Alternatively, a bandage can be applied to secure the lidocaine patch (Figure 4).

**DOSING GUIDELINE**

Based on pharmacokinetic studies conducted by us and others as well as our clinical experience, we recommend the following dosing guideline for lidocaine patches in dogs (Table 1).\(^\text{12,15}\) The patch should be cut to the length of the surgical site and approximately two to three index-finger widths and applied on either side of the surgical incision. If the surgical incision is irregular (e.g., amputation), the patch can be cut into several smaller pieces and applied around the incision for maximal dermal exposure. The key to dosing is remembering that lidocaine patches act locally and the drug is not absorbed systemically. Therefore, patches should be applied near the surgical site and cover the area where pain must be alleviated.

Dosing for the patch largely depends on the size of the site of desired application. Alternatively, animal body weight and size can provide a rough estimate of the number of patches needed. Our dosing guideline for cats is based on our pharmacokinetic study results and clinical anecdotal experience (Table 1).\(^\text{12,15}\) Based on current measured plasma lidocaine concentrations resulting from patch application, the likelihood of systemic toxicosis in cats is low.\(^\text{15}\)

**CONCLUSION**

Lidocaine patch application on dogs and cats appears to be a useful complement to existing pain management techniques involving the systemic use of opioids and NSAIDs (Figure 5). Transdermal patch application results in interference with sodium channel function and induces a differential blockade, preserving sensory function of the skin and motor function of the muscles while inducing analgesia. Studies focusing on the efficacy of lidocaine patch use on dogs and cats are needed.

**REFERENCES**

3. Gammaitoni AR, Alvarez NA, Galer BS: Safety and tolerability of the lidocaine patch 5%. A targeted


15. Ko JCH, Maxwell LK, Abbo LA: Pharmacokinetics of lidocaine following the application of 5% lidocaine patches to cats. Submitted for an oral presentation at the upcoming annual meeting of the American College of Veterinary Clinical Pharmacologists.

### ARTICLE #1 CE TEST

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1. The proposed mechanism of lidocaine is
   a. inhibition of sodium ion movement.
   b. stimulation of action potentials.
   c. interference with calcium channels.
   d. promotion of nerve conductance.

2. Lidocaine is classified as
   a. an α₂-agonist.
   b. an opioid.
   c. a local anesthetic of the amide class.
   d. a dissociative anesthetic.

3. Lidocaine may be administered
   a. topically.
   b. intravenously.
   c. by infiltration.
   d. all of the above

4. Adverse reactions to lidocaine patch application include
   a. mild skin irritation.
   b. seizures.
   c. motor dysfunction when the patch is applied to a limb.
   d. muscle pain.

5. Which statement(s) regarding the lidocaine patch is/are correct?
   a. It relies on high systemic uptake to produce an analgesic effect.
   b. It produces analgesia in approximately 30 minutes.
   c. Drug absorption is related to the surface area covered by the patch and the duration of application.
   d. b and c

6. In humans, the lidocaine patch
   a. blocks motor input.
   b. produces local analgesia in the area of application.
   c. blocks sensory fibers.
   d. causes numbness in the area of application.

7. Compared with fentanyl patches, lidocaine patches
   a. have a higher chance of causing systemic side effects.
   b. have a longer onset time.
   c. are used adjacent to the surgical site or site of pain.
   d. cannot be cut.

8. The duration of effect of the lidocaine patch is at least
   a. 12 hours.
   b. 1 day.
   c. 2 days.
   d. 3 days.

9. In dogs, plasma lidocaine concentrations can be detected ________ after patch application.
   a. immediately
   b. 6 hours
   c. 12 hours
   d. 24 hours

10. Systemic signs of lidocaine toxicosis include
    a. seizures.
    b. cardiovascular depression.
    c. tremors.
    d. all of the above