How to Use Fentanyl Transdermal Patches for Analgesia in Horses

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Fentanyl transdermal patches can provide significant analgesia in horses for a variety of painful conditions, especially those with a visceral component. Patches are applied to clipped skin on the neck or upper forearm under a light bandage. One 10-mg patch per 150 kg of body weight is recommended; patches may be replaced every 48–72 h. Undesirable side effects have not been observed at this dose in any clinical cases. Authors' address: Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610-0136.© 2002 AAEP.

1. Introduction

The choices available for pain management in the equine patient are limited but not necessarily inadequate. Non-steroidal anti-inflammatory drugs (NSAIDs), including phenylbutazone and flunixin meglumine, are commonly used for both their extended duration of analgesia and for management of inflammation, fever, and endotoxemia. Pain associated with the musculoskeletal system is more effectively managed with phenylbutazone, whereas visceral pain, specifically colic pain, seems more responsive to flunixin meglumine. The gastrointestinal and renal side effects associated with NSAIDs are mild and manageable at lower doses but can become significant with higher or more frequent dosing, in foals, or in horses with diseases such as right dorsal colitis, gastric ulcer syndrome, and azotemia. Alpha-2 agonists such as xylazine and detomidine have potent analgesic properties in addition to their sedative effects. These drugs are the most potent analgesics available for equine visceral pain. The often significant side effects of cardiovascular depression and gastrointestinal hypomotility and the short duration of action of the alpha-2 agonists limit their use as analgesics for protracted pain management. Opioids such as morphine are widely used in human and small animal medicine for pain management. However, the use of pure /-agonist opioids in horses has been limited because of the significant undesirable side effects, including increased locomotor activity, excitation, and gastrointestinal hypomotility. Butorphanol, an agonist-antagonist opioid, has been used for visceral and somatic pain in horses, both alone and combined with an alpha-2 agonist. The undesirable opioid effects are less dramatic but still apparent at therapeutic doses. Experimental studies suggest the duration of effect for butorphanol alone varies from 30 min to 4 h; actual clinical analgesia is considered good but short-lived. Missing from the equine veterinari-
an’s pain management option list is a long-acting, potent analgesic with minimal gastrointestinal side effects.

Fentanyl is a \( \mu \)-agonist opioid, approximately 150 times more potent than morphine. The drug’s low molecular weight and high lipid solubility produce a rapid onset and short duration of action when administered parenterally and render it suitable for transdermal dosing. A transdermal “patch” formulation of the drug was developed to meet the needs of human chronic pain patients requiring significant analgesia for extended periods. The fentanyl patch is designed to deliver the drug at a constant rate based on the surface area of the patch and on the anatomic layers of human skin.\(^3\) Recently, this transdermal analgesic system has been adopted by companion animal clinicians for management of post-surgical and cancer pain in hospitalized small animal patients.\(^5\) Several studies have examined the pharmacokinetics of transdermal fentanyl in a variety of species, including cats, dogs, goats, and horses.\(^6\)–\(^10\) Clinical reports on efficacy and side effects are limited, however, especially in large animal patients.

The University of Florida Large Animal Teaching Hospital has been using fentanyl patches in a variety of equine patients requiring analgesia beyond what is available with conventional medications. Subjective assessments of analgesia were included in the daily examinations of these patients and were based on changes in heart rate, respiratory rate, general attitude, appetite, mobility, gastrointestinal function, and other clinical impressions. Patients were also closely monitored for signs of side effects from the opioid, including anxiety, locomotor excitement, gastrointestinal hypomotility, and respiratory depression. Specific attention was paid to the anatomic source of pain involved, i.e., visceral (gastrointestinal, urogenital, pleural), somatic (musculoskeletal, cutaneous), or both, and on whether there was differential improvement when fentanyl patches were used. The intent of daily clinical analgesic assessment during fentanyl patch use was to identify those animals showing notable subjective improvement and to correlate anatomic source of pain with improvement.

2. Materials and Methods

Duragesic® fentanyl transdermal therapeutic systems\(^2\) (patches) are available in 2.5-, 5.0-, 7.5-, and 10.0-mg sizes designed to deliver 25 \( \mu \)g/h, 50 \( \mu \)g/h, 75 \( \mu \)g/h, and 100 \( \mu \)g/h, respectively, in human patients (Fig. 1). The patches were dispensed by the University of Florida Veterinary Medical Teaching Hospital Pharmacy to the prescribing clinician under the State and Federal rules governing CII narcotic drug delivery systems. Equine patients selected to receive fentanyl patches were either receiving NSAIDs at maximum dosage with inadequate analgesia, or NSAID use was contra-indicated. The choice to include fentanyl patch therapy was at clinician discretion; no non-medicated controls or blinding of observers was used in the clinical observation period. Number and size of patches for each patient were based on a recommended dose of one 10-mg patch per 150 kg of body weight for equine patients.\(^9\) Sites on the lateral cervical, and/or lateral or medial proximal antebrachial area were clipped with a No. 40 blade. Some clinicians chose to shave the site using a straight razor to remove hair stubble. The site(s) were prepped using chlorhexidine gluconate 4% scrub and alcohol, although this step proved both unnecessary and perhaps counter-productive for patch adherence and skin integrity. Skin was allowed to dry completely before patch application. The plastic backing was peeled away from the patch, and the adhesive side of the patch placed flat against the clipped skin site. Better adherence was achieved if the patch was held in place with the palm for 30 s to activate the adhesive. Cyanoacrylate glue was used in some cases to adhere the margins of the patch to the skin (Fig. 2). Patch sites were wrapped with Elastikon\(^b\) adhesive tape in not more than two layers circumferentially (Fig. 3). Patch placement and adherence was checked daily. Re-dosing was at clinician discretion but usually occurred at 72-h intervals. For patients requiring re-dosing, new patches were applied over the same site as exhausted patches; re-clipping was not usually necessary with a single re-dosing interval.

3. Results

Table 1 is a summary of clinical cases where fentanyl patches were used as part of pain management. Analgesic assessment was a subjective, collective opinion made by the prescribing clinician and the Anesthesia and Pain Management and Large Animal Medicine Residents (Wegner, Franklin), based
on changes in vital signs, attitude, appetite, mobility, and other factors. Visceral sources of pain included the gastrointestinal and urogenital systems and the pleural and peritoneal surfaces of body cavities. Somatic sources of pain included the musculoskeletal apparatus and skin; laminitic pain was included in this category.

4. Discussion

The inclusion of fentanyl patches as part of pain management in equine clinical cases at the University of Florida Large Animal Teaching Hospital has been limited to date. However, the consistent and often significant improvement in clinical signs of visceral pain in these patients when fentanyl patches were employed supports their continued use. Several researchers have examined the pharmacokinetics of transdermal fentanyl in normal horses, and work is underway to assess analgesia and side effects in a dose-response fashion. Transdermal fentanyl uptake in horses is rapid, likely because of sebaceous gland as well as transdermal passage, with plasma levels over 2 ng/ml within 4 h of patch application. Plasma levels peak at 6–9 h after patch application and remain above 1 ng/ml for up to 54 h after application, but fall rapidly when the patch is removed. When patches were reapplied in 48- to 72-h intervals, average steady-state levels of 1.9 and 1.2 ng/ml, respectively, were obtained. In humans, plasma concentrations over 1 ng/ml are considered analgesic, but wide variations in both uptake from patches and in analgesic effects are seen. The existing pharmacokinetic information supports our clinical approach to dosing for analgesic effect, although replacement of patches every 48 h rather than every 72 h is advised because of the rapid uptake by horses. We were surprised that cases with distinct visceral pain, such as colitis or pleuritis, seemed notably more comfortable, even when doses below 10 mg/150 kg were used. In patients with both visceral and somatic pain, usually those with laminitis secondary to other problems, we noted obvious improvement in the visceral pain, but inconclusive, or only slight improvement in the laminitic pain. This finding is disappointing, because fentanyl seemed a likely addition to the management of laminitis. However, our dosing levels were conservative, and at higher doses, improvement in somatic, and specifically laminitic pain, may be realized. Undesirable side effects such as anxiety, locomotor activity, and gastrointestinal hypomotility were not observed in any clinical case. In those patients with diarrhea, no change in hypermotility or feces consistency was observed as a direct result of fentanyl patch use, though diarrhea did, in some cases, resolve while these animals were being treated with fentanyl patches. Minor skin irritation at the site of the patches was noted in one case (case 6), but this horse also showed sensitivity to other adhesive dressings. Because fentanyl is a potent II narcotic with high abuse potential and severe, life-threatening side effects if taken accidentally by children or small animals, pain management in horses using fentanyl patches should be limited to supervised in-hospital cases. Protocols to prevent possible misuse should include a daily assessment by the prescribing clinician of patch position on the patient and prompt disposal of exhausted patches, also by the responsible clinician. Cost to the client per 10-mg patch is approximately $60.00 from the University of Florida Veterinary Medical Teaching Hospital Pharmacy. This expense must be kept in perspective, because patches are used over a 48- to 72-h period, and when averaged, the cost per day for two patches is approximately $40.00. Our clinical results thus far suggest fentanyl patches have a definite place in

Fig. 2. Fentanyl patches, right partially unbandaged (case 9).

Fig. 3. Fentanyl patch in place, left proximal forearm (case 8).
equine pain management, and we look forward to ongoing clinical and laboratory research to further refine and improve efficacy.

References and Footnotes


Table 1. Clinical Cases with Fentanyl Patches as Part of Pain Management

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Signalment</th>
<th>Painful Problem(s)</th>
<th>Body Weight (kg)</th>
<th>Patch No. and Size (re-dose)</th>
<th>Analgesic Assessment</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10 yr, Morgan, F</td>
<td>Peritonitis, incisional dehiscence, laminitis</td>
<td>520</td>
<td>3 × 10 mg</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>6 mo, TB, M</td>
<td>Colitis, laminitis</td>
<td>250</td>
<td>1 × 10 mg (once)</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>11 yr, TB, MC</td>
<td>Right dorsal colitis</td>
<td>535</td>
<td>2 × 10 mg</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>7 yr, QH, M</td>
<td>Post-ureterolith removal, peritonitis</td>
<td>560</td>
<td>2 × 10 mg</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>3 day, TB, M</td>
<td>Severe flexor contracture</td>
<td>52</td>
<td>1 × 2.5 mg</td>
<td>S: +</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>2 yr, TB, F*</td>
<td>Pleuritis, pleuropneumonia, laminitis</td>
<td>480</td>
<td>2 × 10 mg (once)</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>1 yr, TB, M</td>
<td>SQ emphysema, head neck, chest, limbs</td>
<td>337</td>
<td>1 × 5 mg, 1 × 10 mg (once)</td>
<td>V: + +</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>12 yr, Mini, F</td>
<td>Necrotic vaginitis, peritonitis, laminitis</td>
<td>180</td>
<td>1 × 2.5 mg</td>
<td>V: +</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>2 yr, TB, F*</td>
<td>Post-rib resection, pleuritis</td>
<td>480</td>
<td>2 × 10 mg</td>
<td>V: + +</td>
<td>None</td>
</tr>
</tbody>
</table>

*Same horse, 1-mo interval between treatments.

TB, Thoroughbred; WB, Warmblood; QH, Quarter Horse; Mini, American Miniature Horse; V, visceral pain; S, somatic pain; +++, improvement; +, slight improvement; +/−, inconclusive; −, no improvement.