

Managing Pain in Trauma Patients

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Trauma reliably produces pain, and analgesic therapy should be considered for every animal presented for treatment of injuries. However, many injured human and veterinary patients are not treated with analgesics at all or they receive therapy that is inadequate to meet their needs.¹⁻³ This unfortunate practice has been attributed to many factors, including deficiencies in clinician knowledge, inappropriate attitudes regarding pain and analgesia, and excessive reliance on behavior as an indicator of distressing pain. Perhaps the most important aspects of pain management are to be suspicious that pain is present in any injured animal and to be highly motivated to treat it, particularly in patients so obtunded by their injuries that they may not be able to behave in ways consistent with a response to pain.

Actual or potential tissue injury provokes a neurologic response to injury termed *nociception*. Nociception generates ascending information coded in a manner that is highly likely to be interpreted as pain. Nociceptive information is conveyed to the spinal cord primarily by specialized fiber types including small myelinated A delta fibers (responsible for a fast [phasic] response) and small, unmyelinated, slow-conducting C fibers (responsible for delayed sensation). Other nonnociceptive somatosensory fibers may be recruited into the nociceptive process, particularly consequent to peripheral sensitization associated with postinjury inflammation. Persistent nociception influences central processing of this information and changes how information is processed in the superficial laminae of the spinal cord at the segments involved. These changes include reduction of response thresholds, amplification of responses, and expanded receptive fields.

Although injury predictably activates nociception, pain intensity is often unpredictable and there are dramatic species, breed, and individual differences in response to identical injury. Furthermore, the intensity of reported pain (in humans) or the magnitude of behavioral changes (observed in animals) may not correlate well with observed injury. In a fascinating study of patients admitted to an emergency department, Melzack and associates observed the loose relationship between injury severity and pain felt in the first hours following injury.⁴ Some 40% of patients felt that their pain was disproportionately severe in relation to their injuries, and another 40% were surprised at their relative lack of pain. Only 20% of patients reported that their pain was what they would expect based on self-evaluation of their wounds. These observations reinforce the view that pain intensity may be very difficult to predict and should bias us to assume its presence in all injured animals.

PAIN AND THE STRESS RESPONSE

Injury is followed by responses and adaptations that comprise both the neuroendocrine stress response and behavioral responses designed to limit further injury or facilitate recovery. Pain is a stress resulting from internal or external stressors. When the stress of pain becomes severe enough to produce distress, it becomes a stressor as well.⁵ Thus pain, as both a stress and a stressor, may intensify the physiologic stress response to injury. Although this response is appropriate (and in fact may be essential for recovery), stress that is too severe for the animal to be able to successfully adapt to it becomes distress. The state of distress is associated with maladaptive physiologic responses (including hypertension, gastrointestinal lesions, and immunosuppression) and maladaptive behaviors (restlessness, failure to groom or eat, inability to rest, and others). In patients with limited physiologic reserves, an intense stress response may be associated with increased morbidity and mortality. For example, human neonates undergoing thoracic surgery develop an intense neuroendocrine stress response that has been associated with increased morbidity and mortality.⁶⁻⁸ This response may be blunted by the administration of opioid analgesics, potentially improving survival following thoracic surgery.⁷

MANAGEMENT OF ACUTE PAIN

Pain caused by trauma (whether due to injury or surgery) is considered *acute*. Acute pain generally peaks in intensity within 1 to 2 days after injury and

wanes progressively over the following days to weeks. Therapy of this type of pain typically centers on *prevention, nursing care, and drug therapy*. The concept of prevention is most relevant to surgical trauma, where careful planning and handling tissue in a manner to minimize the amount of trauma are obvious goals. Pretreatment with analgesics (before surgery or at least prior to recovery of consciousness following anesthesia) may also reduce postoperative pain by inhibiting central sensitization. Nursing care and attention to physical needs are essential to optimal care. No analgesic drug therapies can compensate for inadequate nursing! Useful pharmacologic agents include opioids, nonsteroidal antiinflammatory drugs (NSAIDs), and local anesthetics.

Opioid Analgesics

Of the injectable opioids, morphine, oxymorphone, and butorphanol are used most often. These drugs are generally the most effective analgesics for the treatment of moderate to severe pain, particularly acute pain due to trauma and surgery. Therapy with any of these drugs needs to be tailored to the individual animal, as patient response varies among individuals and species and is affected by level of consciousness, intensity of pain and its source, and presence of coexisting disease. All opioid drugs are characterized by dose-dependent analgesia as well as dose-dependent side effects. Potential side effects important to the injured patient include respiratory depression, bradycardia, and hypotension. However, the vast majority of injured patients can tolerate side effects associated with therapeutic doses of these drugs with no adverse effect. Unfortunately, opioids are often needlessly withheld from animals with chest trauma, based on extrapolation from improper physician practices or conclusions of studies with inappropriate controls.⁹

Side effects of opioid agonists include nausea, vomiting, and dysphoria. These are particularly likely to occur when such drugs are administered intravenously to normal dogs. These complications are infrequently observed in sick or injured animals and generally are not difficult to manage if they do occur. Histamine release following administration of morphine could cause systemic hypotension and worsen circulatory shock; therefore oxymorphone may be preferred in hypotensive animals because of its lower propensity to cause histamine release. However, proper fluid therapy will prevent or reverse opioid-induced hypotension in awake animals.

Butorphanol, pentazocine, and nalbuphine are opioid agonist-antagonists. These drugs produce analgesia by agonist action at kappa opioid receptors but are

antagonists at mu receptors. There is a relatively low ceiling on the analgesia and respiratory depression these drugs produce, and the risk of life-threatening hypoventilation is negligible. This therapeutic ceiling limits administration of these drugs to the treatment of mild to moderate pain. Butorphanol is unpredictable as a tranquilizer when given to alert animals, but most depressed dogs and cats are sedated by therapeutic doses. Butorphanol administration produces analgesia at dosages (0.4 to 1.0 mg/kg) that cause minimal cardiopulmonary depression (Table 1). Butorphanol will antagonize the effects of opioid agonists and reverse much of the sedation produced by these drugs. The partial opioid agonist buprenorphine dissociates from mu opioid receptors slowly, yielding a relatively long duration of action.

Opioid agonists should be administered on a fixed schedule every 2 to 4 hours, although the frequency can be increased in patients that require additional analgesia. Analgesics are given intravenously whenever possible to insure distribution of the drug and to avoid painful intramuscular injections. The opioid agonists morphine and oxymorphone should be given "to effect" because of tremendous interpatient variability in dosage requirements. To estimate the dosage requirement, give small intravenous dosages (0.1 to 0.3 mg/kg of morphine [dogs] or 0.05 mg/kg of oxymorphone [dogs, cats]) every 3 minutes until a satisfactory level of analgesia and/or sedation is achieved. The total dosage is then repeated at regular intervals. The peaks and valleys of plasma drug concentrations seen with intermittent intravenous administration can be avoided by administering these drugs via a continuous intravenous infusion: The cumulative dosage is determined, and a slow intravenous infusion is begun immediately at a rate calculated to deliver that dosage over 2 to 4 hours. The animal is reevaluated frequently, and the infusion rate is slowed or increased as needed.

Nonsteroidal Antiinflammatory Drugs

Prostaglandins are produced by the enzyme complex cyclooxygenase (COX). Cyclooxygenase activity may be constitutive (e.g., the isozyme COX-1 produces prostaglandins necessary for maintaining normal metabolic function of many tissues) or induced (e.g., the isozyme COX-2 is induced by inflammation and produces prostaglandins that participate in that process). Prostaglandins are an integral part of the inflammatory response following injury, and these compounds enhance nociception both peripherally and centrally. Once liberated, prostaglandins sensitize C fiber nociceptors and promote the hypersensitivity

Table 1
Drug Dosage Recommendations

Drug	Dose	Comments
Nonsteroidal Antiinflammatory Drugs		
Acetaminophen	Dogs: 15 mg/kg PO q8h Cats: Contraindicated	Minimal antiinflammatory action
Aspirin	Dogs: 10–25 mg/kg PO q12h Cats: 10–25 mg/kg PO q48h	Appropriate for mild analgesia and antiinflammatory therapy; gastrointestinal side effects are likely at higher doses
Carprofen	Dogs: 2.2 mg/kg PO q12h	Safer than most other NSAIDs for use in dogs
Flunixin meglumine	Dogs: 1.1 mg/kg IV, IM, SC, PO q24h for 3 days	Limit use to 3 consecutive days; oral forms not available in the US except as equine granules and paste (50 mg/g)
Etodolac	Dogs: 3–5 mg/kg PO q12–24h	Available in 200 and 300 mg capsules and 400 and 500 mg tablets
Ketoprofen	Dogs, cats: 1 mg/kg PO q24h for 5 days or 1–2 mg/kg IV, SC, IM q24h for 5 days	Tablet in US is 12.5 mg; injectable form is approved for horses; tablets are approved for small animals in Canada
Ketorolac tromethamine	Dogs: 0.3–0.5 mg/kg IV, IM q8–12h for 1–2 doses, 5–10 mg/dog PO (10 mg for dogs weighing >30 kg) Cats: 0.25 mg/kg IM q8–12h for 1 or 2 treatments	Do not use for >3 consecutive days
Meclofenamic acid	Dogs: 1 mg/kg PO q24h for 5 days	Tablets (10 and 20 mg) available for use in dogs; granules are available for use in equines
Naproxen	Dogs: 5 mg/kg once, then 1–2 mg/kg PO q48h	Available as 220 mg over-the-counter tablets and a 25 mg/ml oral suspension
Phenylbutazone	Dogs: 15–20 mg/kg PO q8–12h	Approved for use in cats in the UK at 25 mg/kg q12h for 5 days
Piroxicam	Dogs: 0.3 mg/kg PO q48h	Potent; only available in 10 mg capsules
Local Anesthetic Agents		
Lidocaine 1% or 2%, with or without epinephrine	Constant infusion (dogs): 30–50 µg/kg/min (no epinephrine) Local infiltration Dogs, cats: 0.2–1.0 ml of 1–2% solution SQ for point block Dogs: <6 mg/kg for larger areas Cats: <2 mg/kg for larger areas Epidural Dogs, cats: 3–5 mg/kg of 2% once, to a maximum of 6 ml in dogs	When infiltrating larger areas, use 1% lidocaine with epinephrine (1:100,000) to reduce toxicity and retard absorption
Bupivacaine 0.25% and 0.5%, with or without epinephrine	Local infiltration Dogs, cats: 0.2–1.0 ml of 0.25–0.5% SQ for point block Dogs: <3 mg/kg of 0.25% with epinephrine for larger areas Cats: <1.5 mg/kg of 0.25% with epinephrine for larger areas Interpleural Use 0.25%, with epinephrine Dogs: <3 mg/kg once; 1 mg/kg q6h Cats: <1–2 mg/kg once; 0.5 mg/kg q6h Epidural Dogs, cats: 1.5–2.5 mg/kg as a 0.5% solution for complete anesthesia (maximum of 6 ml) For analgesia with incomplete motor block, reduce to a 0.125% solution and administer 0.1–0.5 mg/kg If subarachnoid injection is performed, use preservative-free bupivacaine without epinephrine	Provides longer lasting analgesia than lidocaine (4–6 hours vs. 1 hour). Use undiluted 0.25% solution if the chest tube is positioned near the site of injury; otherwise dilute with sufficient volume of saline to reach entire pleural space (e.g., dilute to 10–30 ml) Use preservative-free bupivacaine for epidural administration; may be combined with morphine or other opioids for epidural or spinal administration; reduce subarachnoid dose to 30% of epidural dose

(continued)

Table 1 (continued)
Drug Dosage Recommendations

Drug	Dose	Comments
Opioids		
Morphine	Systemic Dogs: 0.2–2.0 mg/kg IV, IM, SQ q4h	For titration of IV dose, administer 0.1–0.5 mg/kg at a time and repeat every 5 minutes to effect; stop titration if mydriasis occurs in the cat
15 mg/ml injection		
1 mg/ml preservative-free injection	Cats: 0.1–0.4 mg/kg IV, IM, SC q4h	
Oral tablets, elixirs	Dogs: 1–5.0 mg/kg PO q4–6h Epidural Dogs, cats: 0.1–0.2 mg/kg q8h	One-time administration of injectable morphine appears safe despite the presence of potentially neurotoxic preservatives; injectable morphine should be diluted in saline to 1–2 mg/ml; for repeated administration, use undiluted preservative-free morphine; for intrathecal injection, use preservative-free morphine at one third the epidural dose; may be combined with local anesthetics or demetomidine
Oxymorphone	Systemic Dogs: 0.05–0.2 mg/kg IV, IM, SQ q2–4h Cats: 0.025–0.1 mg/kg IV, IM, SQ Epidural Dogs, cats: 0.05–0.2 mg/kg q8h	To titrate IV therapy, use the lower doses and administer as for morphine May be combined with local anesthetics for epidural use
Fentanyl injection	Dogs, cats: 20–40 µg/kg IV, IM, SQ q1h or as a continuous IV infusion	Lower doses may provide analgesia when combined with other drugs; higher doses administered as a continuous infusion may be used as part of a general anesthesia protocol; fentanyl may be administered epidurally once with morphine to speed the onset of analgesia
Fentanyl transdermal	Cats: 25 µg patch Dogs: <10 kg: 25 µg 10–29 kg: 50 µg >30 kg: 75–100 µg or more	Latency to stable therapeutic plasma concentrations is at least 6–12 hours in cats and 12–24 hours in dogs; some animals never reach therapeutic plasma concentrations
Meperidine	Dogs: 5–10 mg/kg IM, IV q0.5–2h Cats: 3–5 mg/kg IM, SQ q2–4h	Not recommended due to short duration of action and cardiovascular depression when administered IV
Codeine	Dogs: 0.5–2 mg/kg PO q4–8h	Inexpensive for use in dogs only when combined with acetaminophen or aspirin; in that case, use tablets with 60 mg of codeine and 300 mg NSAID and administer at 5–10 mg/kg of the NSAID q8h
Butorphanol	Dogs, cats: 0.1–1.0 mg/kg IV, IM, SC q1–2h (dogs), q2–6h (cats) Cats: 0.5–4.0 mg/kg PO q6–8h	Agonist-antagonist drug; sedation lasts longer than analgesia in the dog; may be used to reverse mu effects of agonist drugs
Pentazocine (injectable/oral)	Dogs: 1–3 mg/kg IV, IM, SQ q1–6h, 2–10 mg/kg PO q4–6h	Agonist-antagonist drug
Nalbuphine	Dogs: 0.1–1.0 mg/kg IV, IM, SQ	Agonist-antagonist drug
Buprenorphine	Dogs: 5–20 µg/kg IV, IM, SQ, epidural q6–8h Cats: 5–10 µg/kg IV, IM, SQ, epidural q6–8h	Partial agonist

that follows inflammation. This phenomenon accounts in part for the prolonged tenderness of an injury. NSAIDs inhibit production of prostaglandins, and the bulk of their efficacy as analgesics is attributed to their local antiinflammatory effects and inhibition of central nervous system prostaglandin formation.

Side effects of most available NSAIDs limit their usefulness in the treatment of unstable injured pa-

tients. Side effects including gastric and duodenal ulceration and renal ischemia are much more likely in animals with poor visceral blood flow, a common condition in hemodynamically unstable patients. Therefore it may be best to delay therapy with any of these drugs until normal circulation is restored. Newer NSAIDs (e.g., carprofen and etodolac) and acetaminophen weakly inhibit COX-1 and appear to be much less likely to produce ischemic renal injury or

gastrointestinal ulceration than ones that preferentially inhibit COX-1. These drugs may be particularly useful as therapy for acute pain in the days following initial stabilization.

Local Anesthetics

Useful local anesthetic agents include lidocaine and bupivacaine. The advantages of local and regional anesthesia for acute pain management include the potential for complete analgesia, blunting of the neuroendocrine stress response, and minimal cardiovascular and respiratory depression. The local anesthetic agents are useful for prevention and management of procedural and operative pain. Local infiltration at a surgical site may provide superior postoperative analgesia for some superficial procedures compared to general anesthesia alone.^{10,11} Lidocaine (1% to 2%) is effective in preventing the pain associated with intravenous catheterization, aspiration of body cavities, minor skin surgeries, and other procedures. The sting of injected lidocaine may be reduced by mixing one part sodium bicarbonate (1 mEq/ml) with nine parts 1% to 2% lidocaine just prior to injection.¹² This combination dramatically improves patient tolerance of the local anesthetic injection and may hasten the onset of anesthesia. Lidocaine with epinephrine (1:100,000) will provide local anesthesia for longer periods (up to 1 hour or more) than lidocaine alone.

Interpleural or intercostal administration of bupivacaine (0.25% to 0.5%) with epinephrine appears to provide reasonable analgesia in dogs following rib fractures or thoracic surgery.^{13,14} Bupivacaine may be periodically administered directly through the chest tube or may be administered continuously via a long catheter tunneled through the chest tube. The latter technique allows continuous administration without interference with a closed collection system.¹⁵ The cumulative daily dose of bupivacaine in healthy dogs should not exceed 8 mg/kg on the first day and 4 mg/kg on subsequent days.¹⁶ In clinical practice, daily doses of 2 to 4 mg/kg are generally sufficient.

Lidocaine has a short duration of action and is used for anesthesia to facilitate short procedures. Intravenous lidocaine (2%) without epinephrine may be useful as a systemic analgesic in dogs; although it has been shown to have clinical benefit in humans and will reduce anesthetic and opioid requirements,¹⁷ it does not appear to be effective as a sole agent in dogs. It may be used as an adjunct to other analgesic techniques and is administered at a dosage of 1 to 2 mg/kg followed by a continuous infusion at the rate of 1.5 to 3 mg/kg/hr.

Bupivacaine has a longer duration of action than li-

docaine and is useful for relief of pain following surgery or trauma. Administration of bupivacaine with epinephrine (1:100,000) will provide local anesthesia for up to 6 hours. For treatment of thoracic wall pain, 0.25% bupivacaine can be infiltrated near the proximal intercostal nerves along the caudal border of each rib. Several intercostal nerves on either side of an incision or fracture should be blocked. Alternatively, undiluted bupivacaine (0.25% or 0.5%; up to a maximum of 1 to 2 mg/kg every 6 hours) can be administered through a chest tube into the affected side. A slow infusion rate will limit any pain associated with drug administration. The most effective anesthesia occurs where the drug pools prior to absorption; hence it is important that the treated side be placed down.

Epidural Analgesia and Anesthesia

Although epidural anesthesia has been used successfully in veterinary medicine since early in this century, interest in this technique waned following the widespread introduction of inhalation anesthesia in clinical practice. The discovery in 1976 that analgesia in animals could be obtained by intrathecal injection of opioids stimulated keen interest in epidural analgesia in humans and has renewed veterinary interest as well.¹⁸⁻²² Currently, local anesthetic agents, various opioids, and alpha-2 adrenergic agents are administered by epidural or intrathecal (subarachnoid) injection in companion animals.

Indications for Epidural Analgesia

Veterinarians have long used epidural administration of local anesthetics to facilitate anesthesia for surgery including cesarean sections and orthopedic repairs of the pelvis or hindlimbs. More recently, epidural administration of opioids and/or local anesthetic agents has been used for postoperative analgesia. However, the indications for use of these techniques in companion animals remain to be defined. Although there have been many clinical investigations into the advantages and disadvantages of spinal analgesia in humans, only a few reports describing similar studies in dogs have been published. The drug therapy options most widely used at this time include single injections of opioids, local anesthetics, or combinations of the two. Repeated or continuous administration of these agents may be performed with an epidural catheter. Techniques of epidural drug administration have been reviewed.^{23,24}

Spinal opioids are usually administered for intraoperative and postoperative analgesia, but may also be useful for more prolonged treatment. Of the available

opioids suitable for epidural injection, morphine is most useful for analgesia of the upper abdomen and thorax because of its low lipid solubility and ability to diffuse further cranially. Single preoperative injections of opioids may provide at least some postoperative analgesia for up to 12 to 24 hours following injection. Although spinal analgesia is potentially useful for management of many patients, it may be particularly advantageous in animals in which sedation or other central effects are undesirable and a rapid return to function postoperatively is important.

Patient factors that may be relative or absolute contraindications to spinal analgesia include coagulopathies, bacteremia, severe systemic infection, infection at the site of needle placement, thoracolumbar neurologic deficits, lumbosacral fractures or dislocations, and uncorrected hypovolemia. Potential complications of spinal analgesia include infection, epidural or intrathecal hemorrhage, spinal or nerve root trauma, motor blockade, migration of agents to the brain with pronounced central effects, and persistent weakness or ataxia. Serious complications appear rare when the technique is administered by clinicians skilled in the required techniques.

Bupivacaine is the most useful local anesthetic for epidural use in the dog or cat. Single injections of a 0.25% to 0.5% solution will provide surgical anesthesia for up to several hours. Administration of lower concentrations (0.06% to 0.125%) may provide analgesia without complete motor block. To achieve these lower concentrations, 0.25% bupivacaine may be diluted with an appropriate volume of an opioid such as preservative-free morphine (1 mg/ml).

The opioids most often administered spinally to dogs and cats include morphine, oxymorphone, buprenorphine, and fentanyl. The analgesic activity of spinally administered opioids is attributed to opioid receptor binding in the superficial laminae of the dorsal horn of the spinal cord segments. Thus epidurally administered opioids must cross the dura to gain access to the cerebrospinal fluid and subsequently the spinal cord. Analgesia is produced by modulation of spinal cord processing of nociceptive information without significant central effects or motor, sensory, or sympathetic blockade.

Morphine is the most hydrophilic opioid. This characteristic delays the spinal and systemic absorption of the drug and accounts for the observations that the peak analgesic effect may not be reached for 90 minutes following injection and that some analgesia may persist for up to 24 hours. In contrast to local anesthetics, the extent of spinal analgesia achieved with morphine appears to be relatively independent of the

volume in which it is administered. When relying on it for postoperative pain management, it is important to administer it immediately after the induction of general anesthesia and prior to surgery because of the relatively long latency to peak analgesia.

Fentanyl is very lipid soluble and rapidly absorbed. These characteristics result in an onset of action within minutes of epidural injection and prevent spinal analgesia from extending more than a couple of cord segments on either side of the injection site. There is rapid systemic absorption with central effects. When combined with morphine, epidural fentanyl greatly reduces latency to analgesia, a feature that is useful for management of intraoperative pain.²⁵

The most common side effect of spinal analgesia with opioids reported in humans is pruritus at affected dermatomes, and the most serious side effect is delayed respiratory depression. Patients destined to develop delayed respiratory depression following epidural morphine may not show evidence of this for up to 24 hours after administration. Although uncommon (<2% of patients), delayed respiratory depression may be severe and is the principal reason for close monitoring of human patients following epidural opioid administration. Delayed respiratory depression has not been reported in the dog or cat.

Common side effects of epidural opioids in the dog include weakness of the detrusor muscle and urine retention following administration of morphine or fentanyl and ataxia. The ataxia is usually very subtle and goes unnoticed. Urine retention can become quite problematic for some dogs and may require catheterization. Compared to other opioid agonists, urine retention is less severe following administration of buprenorphine.²⁶

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