Best Practices in Pain Management

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The pain experience
Pain serves an important role in the interaction between the individual animal and its environment in that it signals the potential for tissue damage, and is thus protective in nature.

Nociception consists of transduction (transformation of noxious stimuli into electrical signals called action potentials), transmission (sensory impulses are conducted to the spinal cord), modulation (impulse amplification or suppression within the spinal cord), projection (impulses are transmitted to the brain), and perception (integration, processing and recognition of nociceptive information). The different drugs utilized for pain management target different points along the pain pathway.

It is helpful to determine the mechanism, origin and severity of pain, as this may help in determining treatment options. The mechanism of pain can be due to inflammation, nerve injury, cancer, or idiopathic. Pain may be visceral (organ pain, e.g. peritonitis) or somatic (superficial e.g. skin laceration, or deep e.g. tibia fracture). Some diseases or surgeries may result in more than one of these types of pain (e.g. ovariohysterectomy will have components of somatic pain e.g. skin and muscle and visceral pain e.g. ovaries and uterus).

Injectable analgesics
Opioids
Determining which opioid to use will require an adequate assessment of current pain status and expected pain from the procedure or condition, duration of action, side effects including sedation, nausea and vomiting, hyperthermia (in cats), and cost of the drug.

Morphine
Morphine is a µ opioid receptor agonist that provides analgesia for mild to severe pain. Typical doses range from 0.1 to 0.4 mg/kg IV, IM, or SQ. Duration of action is 4 to 6 hours. Morphine may also cause a release of histamine and should be avoided in patients with mast cell disease. Vomiting may occur and mild to moderate sedation is common following morphine administration. Morphine has been associated with hyperthermia in cats, which in most cases is mild and self-limiting.

Oxymorphone
Oxymorphone is a µ opioid receptor agonist and provides analgesia for mild to severe pain. Doses range from 0.05 to 0.1 mg/kg IV, IM, or SQ. Duration of action is 2 to 4 hours. Vomiting and salivation may occur, and mild to moderate sedation is common following oxymorphone administration.

Hydromorphone
Hydromorphone is a µ opioid receptor agonist and provides analgesia for mild to severe pain. Doses range from 0.05 to 0.2 mg/kg IV, IM, or SQ. Duration of action is 2 to 4 hours. Vomiting and salivation may occur, and mild to moderate sedation is common following hydromorphone administration. Hydromorphone has also been associated with hyperthermia in cats.

Fentanyl
Fentanyl is a µ opioid receptor agonist and provides analgesia for mild to severe pain. The duration of fentanyl from a single IV bolus is approximately 15 minutes, and as a result, fentanyl is often administered as a constant rate infusion. Fentanyl is administered as a single bolus of 2 µg/kg IV, as a CRI in awake patients at 2 to 5 µg/kg/hr, and as a CRI in anesthetized patients at 5 to 10 µg/kg/hr. Vomiting and salivation may occur, and mild to moderate sedation is common following fentanyl administration, though dysphoria may also occur with fentanyl. Fentanyl has been associated with hyperthermia in cats, which in most cases is mild and self-limiting.
Methadone
Methadone is a µ opioid receptor agonist and NMDA antagonist and provides analgesia for mild to severe pain. Typical doses range from 0.1 to 0.4 mg/kg IV, IM, or SQ. Duration of action is 4 to 6 hours. Methadone has been associated with bradycardia in some patients. Vomiting and sedation are uncommon following methadone administration.

Buprenorphine
Buprenorphine is a partial µ opioid receptor agonist and provides analgesia for mild to moderate pain. The dose range of buprenorphine is 0.005 to 0.02 mg/kg IV or IM. Subcutaneous administration may be associated with variable uptake in most patients. Duration of action is 6 to 12 hours. Buprenorphine does not typically result in vomiting or excessive sedation.

Butorphanol
Butorphanol is a κ opioid receptor agonist and µ receptor antagonist and provides analgesia for the mildest of pain. The dose of butorphanol ranges from 0.1 to 0.2 mg/kg, and can be administered IV, IM, or SQ. Duration of action is up to 1 hour.

Alpha-2 Agonists
Dexmedetomidine
Dexmedetomidine administration results in variable analgesia and sedation. Doses of dexmedetomidine range from 0.01 to 0.02 mg/kg IM in dogs at cats.

Ketamine
Ketamine
Ketamine is an NMDA receptor antagonist and may provide an effective analgesic adjunct in patients with hyperalgesia. Ketamine should not be administered as the sole analgesic and does not provide any muscle relaxation. Ketamine should be used in combination with opioids and a muscle relaxant. Single 3 to 5 mg/kg doses of ketamine can be administered IM to cats. The CRI dose of ketamine ranges from 1 to 2 µg/kg/minute.

MLK and DMLK in dogs
Morphine-Lidocaine-Ketamine or Dexmedetomidine-MLK
Morphine, lidocaine, and ketamine can be combined for an infusion for dogs with severe pain or to decrease inhalant anesthetic concentrations during surgery. In a 500 ml bag of LRS, we add morphine (24 mg), lidocaine (300 mg), and ketamine (60 mg), and administer at 2.5 ml/kg/hr in awake patients, and 5 ml/kg/hr in anesthetized patients. At 5 ml/kg/hr, this results in infusions of morphine (0.24 mg/kg/hr), lidocaine (3 mg/kg/hr), and ketamine (0.6 mg/kg/hr), and if added, infusion of dexmedetomidine at 0.5 µg/kg/hr.

Epidurals
Lumbosacral Epidural
In most canine patients, the lumbosacral space can be easily palpated. The spinal cord ends at L5-L6 in most dogs. The spinal cord in cats ends between L6 and S2, so it is possible to puncture the intrathecal space in cats. As such, the cranial spread of drug may result in negative side effects. Local anesthetic drugs should be used with caution when performing epidurals in cats.

Morphine
Use of morphine for epidural analgesia is associated with few systemic side effects and prolonged analgesia (up to 12 hours). The dose of morphine is 0.1 mg/kg diluted with saline to achieve a total epidural volume of 0.2 ml/kg. Alternatively, preservative free morphine can be used at a dose of 0.1 mg/kg and does not need to be diluted. In the event that the intrathecal space is punctured, a spinal may be performed using ½ the dose of preservative free morphine (e.g. 0.05 mg/kg).

Coccygeal epidural in cats
Coccygeal epidurals can be performed under sedation or general anesthesia and are performed at the level of the sacrococcygeal space or between the first and second coccygeal vertebrae. The epidural space is penetrated using a 25-gauge needle. There are no clinical studies on efficacy of the coccygeal epidural technique.
**Lidocaine**
Coccygeal epidurals in cats using lidocaine typically result in a fast onset of analgesia (approximately 5 minutes) and a duration of approximately 1 hour. The dose used for caudal epidurals in cats is 0.1 to 0.2 mL/kg using a 2% solution.

**Morphine**
Morphine can also be used for coccygeal epidural administration. The dose of morphine is 0.1 mg/kg diluted with saline to achieve a total epidural volume of 0.2 ml/kg. Alternatively, preservative free morphine can be used at a dose of 0.1 mg/kg and does not need to be diluted.

**Techniques for chronic pain management**

**Fentanyl Patches**
Fentanyl patches are available in various sizes and have been associated with minimal side effects in healthy small animal patients. Placement of fentanyl patches on the nape of the neck may be one option for provision of analgesia. Fentanyl patches should be placed at least 12 hours prior to surgery or other analgesia should be provided for 12 hours if patches are placed at the time of surgery. Fentanyl patches have been associated with sedation following surgery, and have been associated with dysphoria when placed prior to surgical procedures.

Sizes of fentanyl patches range from 10 to 100 mcg/hr. In small patients, keep half of the patch covered with adhesive to decrease dermal absorption – do not cut the patch.

**Lidocaine Patches**
Lidocaine patches are adhesive patches that contain lidocaine and can be applied over or alongside incisions. Several studies have demonstrated that systemic absorption is variable, but tends to be low. Patches are effective for 24 hours, can be cut to be appropriate for the application site, and can be replaced after 24 hours.

**Transdermal Fentanyl**
A transdermal formulation of fentanyl for topical administration in dogs is available. The solution is a proprietary formulation that is applied over the neck area in dogs. Analgesia lasting up to 4 days has been demonstrated following surgery.

**Oral Transmucosal (OTM) buprenorphine**
Oral transmucosal administration of buprenorphine may be associated with appropriate pharmacokinetics and pharmacodynamics in dogs, though there is considerable variation in response to OTM administration of buprenorphine when administered for post-operative analgesia following ovariohysterectomy. OTM administration of buprenorphine may be more consistent in cats. Doses of buprenorphine for OTM administration in dogs range from 0.02 to 0.12 mg/kg. Doses of buprenorphine for OTM administration in cats range from 0.01 to 0.02 mg/kg up to 3 times daily. Dysphoria, sedation, and salivation can occur following OTM administration of buprenorphine.

**Oral Transmucosal (OTM) methadone**
Methadone has recently been investigated as an option of OTM administration for the treatment of mild to severe pain in cats. The recommended dose of methadone for OTM administration is 0.6 mg/kg, which provides analgesia for 2 to 4 hours, but may last up to 8 hours in some cats. Sedation, bradycardia, and decreased respiratory rate were reported. Euphoria also occurred in some cats.

**Oral drug administration**

**Tramadol**
Tramadol inhibits uptake of serotonin and norepinephrine, and binds to µ opioid receptors, though it is not an opioid. Oral administration of tramadol has been associated with analgesia and mild sedation. Doses of this drug for small dogs are incompatible with drug formulation. Home administration of this drug in cats has been problematic for owners due to the foul taste of this drug and that doses are incompatible with drug formulation. Compounding pharmacies have attempted to provide this drug in liquid format for ease of administration and dosing to cats, but most cats still do not tolerate the taste of the drug. Suggested doses of tramadol are 1 – 4 mg/kg PO up to 4 times daily for dogs or cats. Suggested doses of tramadol are 1 – 4 mg/kg PO up to 4 times daily for dogs.
Gabapentin
Gabapentin is used for the treatment of neuropathic pain and is most often used in conjunction with other drugs. Doses typically range from 2.5 to 10 mg/kg PO twice daily. Sedation may occur as a side effect of this drug.

Amantadine
Amantadine is an anti-viral drug that has NMDA-receptor antagonist properties. Typically used for neuropathic pain and chronic pain in humans, its efficacy has not been well documented in veterinary patients. Amantadine is not typically used alone for analgesia; it is most often used in conjunction with other drugs. Typical dose for amantadine is 3-5 mg/kg PO once per day. This drug should be used with caution in dogs and cats with renal disease.

Tapentadol
Tapentadol is a novel analgesic in that it is a mu opioid receptor agonist that also decreases norepinephrine reuptake at nerve endings. The dual activities of tapentadol have been purported to result in increased analgesia with an opioid sparing effect and decreased side effects compared with other pure mu agonist opioids. While there have been anecdotal reports of tapentadol administration to dogs for pain management, there are no studies documenting the analgesic efficacy of tapentadol in dogs. One study evaluating the pharmacokinetics of tapentadol in dogs utilized a dose range of 5.7-15.75 mg/kg orally. No studies have been performed on the use of oral tapentadol in cats.

Cats and NSAIDS
Meloxicam
Meloxicam is approved for single dose administration subcutaneously (0.3 mg/kg) in cats.

Robenacoxib
Robenacoxib (1 mg/kg) is approved for oral use in cats weighing at least 5.5 lbs and 6 months of age or older, for up to three days for the treatment of pain and inflammation associated with orthopedic surgery, OHE, and castration.

References
2. Gaynor JS, Muir WW. Handbook of veterinary pain management.