

Practical Pain Management in Animals

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Abstract

Assessment of the degree of acute pain being suffered by an animal is difficult; diagnosis of chronic pain is even more challenging. It is far better to predict and prevent (or at least minimise) likely pain than to treat it once established. A “balanced” approach to the management of pain, where the pain pathway is modulated at as many points as possible, will be illustrated by case studies of acute and chronic pain taken from clinical practice. This will highlight the potential for combining anti-inflammatory drugs, local and regional analgesic techniques, various strategies for opioid administration, NMDA antagonists, anxiolytics and physical measures to optimise patient comfort.

How can you tell if the patient is experiencing pain?

▪ **Anthropomorphism**

Prediction of the likely severity of untreated pain arising from a surgical procedure may be made on the basis of the amount of damage that will be caused to the tissues and the anatomical site of the proposed surgery injury. Some extrapolation from human experience (anthropomorphism) is valid. If a procedure will cause pain in a human then it is likely to do so in our patient.

▪ **Unprovoked Behaviour**

- vocalisation (acute pain)
- absence of some normal behavioural patterns such as grooming & play
- attempts to escape (acute pain)
- changes in normal sleeping patterns
- changes in appetite
- changes in temperament, increase in anxiety & fear , quiet/withdrawn (especially with chronic pain)
- guarding or protecting the affected area (patients with chest pain tend to breathe shallowly. Abdominal or back pain results in splinting of abdominal muscles)
- - self mutilation (eg. biting, chewing, scratching. This may be directed at the painful area or it may be a “redirected” behaviour)
- lameness, limb disuse, unusual posture, slow movement, turning head towards painful stimulus, restlessness.

▪ **Behavioural responses to external stimuli.**

- interaction with humans,
- response to gentle handling of surgical site.

- **Clinical signs** (usually not seen with chronic pain)
 - increased heart rate
 - increased blood pressure
 - peripheral vasoconstriction (pallor of mucous membranes)
 - cardiac dysrhythmias
 - sweating (in applicable species)
 - hyperventilation
 - reduction in peristalsis

NOTE: Assessment of behavioural changes rely heavily on a knowledge of what is normal behaviour for the species and, if possible, knowledge of the normal behavioural patterns of the particular individual. For example, dogs will usually demonstrate more overt expression of pain than will cats or herd herbivores such as sheep. When assessing pain in the immediate post operative period, allowance must be made for residual CNS depression from the anaesthetic and the effect of any hypothermia which may have occurred during the anaesthetic period.

When is pain relief appropriate?

Whenever tissue is disrupted pain will usually follow, therefore appropriate pain relief should be given for all but the most trivial surgery. Pain is one condition that should be treated on suspicion. If more than trivial surgery is to be performed, the question is not "Should pain relief be given?", but "What is the best way to provide effective analgesia?"

When should the administration of analgesics begin?

There can be no doubt the patient should not be allowed to recover from anaesthesia before analgesics are effective. Giving appropriate analgesics as part of the anaesthetic technique will reduce the doses of general anaesthetic agents required and thereby reduce the magnitude of cardiovascular depression.

Experimental studies have shown that administration of analgesics before the application of nociceptive stimulus will limit the excitation of dorsal horn neurones in the spinal cord that would otherwise occur ("pre-emptive analgesia"). This implies that less post-operative pain may be experienced if analgesics are given before, rather than after, the surgical incision. The results of clinical investigations of pre-emptive analgesia have been variable, with some studies claiming to demonstrate a beneficial effect while others have been unable to do so.

For how long should pain relief be given?

The administration of analgesics should continue until the clinician is certain that the level of pain has fallen to one that the patient is happy to tolerate. After major surgery this is most unlikely to be less than about twenty four hours and it may be necessary to administer potent narcotic analgesics for 48 -72 hours or longer. Less potent analgesics such as NSAIDs alone may then be adequate.

General strategies for pain control.

Pain can be controlled by interventions aimed at different points in the pain transmission pathway, for example:

- **Limitation of nociceptor stimulation.** This may be achieved by gentle handling and minimisation of tissue trauma. Pre-operative administration of NSAID's such as ketoprofen or carprofen will inhibit cyclooxygenase and thereby reduce the production of prostaglandins and other substances that will sensitise the nociceptors.
- **Interruption of peripheral neural transmission** by the use of local anaesthetics for infiltration of the surgical site, nerve blocks or intravenous regional analgesia.
- **Inhibition of nociceptive transmission at the spinal cord** may be achieved by systemic, epidural or subarachnoid administration of opioids and alpha2 adrenergic agonists, and epidural or subarachnoid administration of local anaesthetics.
- **Modulation of brain pathways** by systemically administered opioids, alpha2 adrenergic agonists and, to a lesser extent, some NSAID,s.
- **“Balanced” or “Multimodal” analgesia** refers to the simultaneous use of a number of the above strategies to maximise pain control with minimal doses of drugs, thereby reducing the likelihood of clinically significant side effects eg.
 - The infiltration of the surgical site with local analgesic combined with the systemic administration of a NSAID and an opioid.
 - Epidural administration of a mixture of bupivacaine and morphine together with systemic administration of a NSAID
- **Additional considerations.**

Ensure that the patient is normothermic and has comfortable bedding and is free from environmental disturbances. Anxiety and fear are limbic and cortical responses to pain which are thought to magnify the hypothalamic neuroendocrinological response to pain. A caring attitude, softly spoken words and judicious use of tranquillisers will often help allay a patient's anxiety. Remember that analgesics are not the best treatment for the discomfort produced by distension of the bladder!

Selection and techniques of administration of individual analgesic drugs.

▪ **Local analgesics**

Compared with lignocaine, bupivacaine is 4 times as potent and lasts about 4 times as long. The onset of action of bupivacaine is slower than lignocaine.

- *Nerve blocks* eg. submandibular block for mandibulectomy
eg. brachial plexus block for surgery distal to lower humerus.
(For best effect, blocks should be performed before AND after surgery.)

- ***Local intravenous regional***

This technique is particularly appropriate if the surgical procedure calls for the use of an Esmarch's bandage or a tourniquet. The analgesia thus provided does not persist for long after the circulation to the limb has been restored, thus other techniques should be used to provide adequate post-operative analgesia. The local analgesic of choice is either prilocaine or lignocaine.

- ***Epidural local anaesthesia***

Local anaesthetic (0.5% bupivacaine or 2% lignocaine) is injected at the lumbosacral space. The area of analgesia is dependent on the volume of solution injected. A volume of 0.2 ml.kg⁻¹ will desensitise the pelvis and hind limbs. The duration of analgesia will be about 1 to 1.5 hours for lignocaine and 4 to 6 hours with bupivacaine. The onset of analgesia is slower for bupivacaine (20 - 40 minutes) than for lignocaine (10 - 20 minutes). Careful attention should be paid to providing adequate analgesia as the epidural blockade wanes.

The complete analgesia and muscle relaxation provided by epidural local analgesia is sufficient to allow the performance of surgery in a conscious patient. In order to keep the patient still it is usually necessary to use heavy sedation or very light general anaesthesia. Many anaesthetists prefer light general anaesthesia as this allows control of the patient's airway, facilitates the administration of supplemental oxygen and permits a more rapid recovery.

Epidural local analgesics may block the efferent impulses from the sympathetic chain resulting in vasodilation of the innervated area with consequent hypotension. The greater the cranial spread of the local analgesic the greater is the risk of significant hypotension developing. To minimise this risk the following steps should be taken.

- Avoid injection of volumes greater than recommended above.
 - Administer I/V fluids during the surgery and give 20 ml.kg⁻¹ rapidly as the block is taking effect.
 - Replace each ml of blood lost with three ml of crystalloid (eg Hartman's solution) or 1 ml of colloid (eg Haemaccel).
 - Keep the depth of general anaesthesia as light as possible.
- *Intra-articular.* Bupivacaine is usually used. The rate of systemic absorption is similar to that from the epidural space.

- **Opioid analgesics.**

- *Systemically administered opioids.*

After an initial pre-surgical dose of opioid, further doses may be titrated against the degree of nociceptive stimulation during anaesthesia or against pain once the patient is conscious. This approach avoids the production of unnecessary respiratory depression.

The selection of the particular opioid and the initial dose rate should be made on the basis of:

- *The expected intensity of the pain.* The pure agonist drugs (eg. morphine, methadone, pethidine, fentanyl) are able to provide more intense analgesia than is obtainable from the partial agonist drugs (eg. butorphanol, buprenorphine, pentazocine).
- *The duration of action required.* Buprenorphine is the longest acting opioid currently available (6 - 8 hrs). Morphine and methadone have a moderate duration of action (about 4 hours). Short acting opioids include pethidine and butorphanol (about 1 hour) and fentanyl (about 20 minutes). Due to its relatively poor lipid solubility, morphine has the longest duration of action in the epidural space (12-23 hours).
- *The desired speed of onset* Compared with intramuscular and subcutaneous routes of administration, the intravenous route usually offers a faster rate of onset of analgesia and a more intense peak effect.

Pethidine should not be given intravenously due to the risk of histamine release and consequent hypotension. Intravenous doses of morphine greater than 0.2 mg/kg are likely to release histamine. There is no difference between I/V and I/M routes on the time of onset of buprenorphine, although the analgesia lasts longer with I/M or S/C injection. Although morphine does act more quickly after I/V injection, the speed of onset is slow compared to other opioids, the full effect not being seen for at least 10 minutes. Methadone and fentanyl act rapidly after I/V administration and are very useful for intravenous premedication.

- *Side effects* The opioids cause little depression of myocardial contractility however all (except pethidine) will increase vagal tone and cause a slowing of heart rate which may be counteracted by the administration of atropine. Opioids generally cause an increase in smooth muscle tone in the gastrointestinal tract. This may cause the passage of faeces or flatus (notably after fontanelle). Vomiting commonly occurs within five to ten minutes of subcutaneous or intramuscular administration of morphine but rarely after the other opioids. Opioids will occasionally initiate panting in dogs since these drugs reset the thermoregulatory "set point". Respiratory depression is a common feature of opioids, although this is unlikely to be a

clinical problem if the drugs are titrated against the pain in incremental doses.

▪ ***Epidural Morphine***

Morphine injected into the epidural space can provide excellent analgesia of the pelvis and hind limbs (together with some analgesia of the thorax) for 6 to 12 hours. There is very little accompanying CNS depression. Some analgesia has been reported after 23 hours.

Epidural injection is best performed after the induction of general anaesthesia but before the start of surgery. It may take up to 40 minutes before the analgesia is fully developed. (Faster onset of analgesia may be obtained by combining pethidine 1 mg/kg with morphine 0.1 mg/kg).

It is recommended that preservative free morphine be used and that it should be diluted with sterile 0.9% saline to give a total volume of 0.2 ml.kg⁻¹.

Of the side effects sometimes seen in humans (nausea, vomiting, delayed respiratory depression, pruritus and urinary retention) only urinary retention and pruritus are occasionally seen in dogs.

▪ ***Intra-articular opioids***

The number of opioid receptors in the joint increases with inflammation. Pharmacokinetics of opioids in the intra-articular space are similar to pharmacokinetics in the epidural space, therefore morphine is likely to be the most satisfactory opioid for intra-articular use. Morphine may be combined with bupivacaine for this application.

- ***Transdermal fentanyl*** Fentanyl patches (100 mcg/hour) applied to the skin allow transdermal absorption of fentanyl. Steady state plasma concentrations are achieved after 24 hours but there is large variation between individuals in the actual plasma concentration of fentanyl that is achieved. Plasma concentration of fentanyl falls rapidly after removal of the patch. It is usually advised to place the patch 24 hours before the surgery for dogs and 12 hours before surgery for cats. Duration of useful analgesia is usually about 3 days.

Dose for dogs:

WEIGHT OF DOG (KG)	FENTANYL PATCH (MCG/HOUR)
<10	25
10-20	50
20-30	75
>30	100

- *Sustained release morphine tablets* (eg MS-Contin) Useful in the management of severe long term pain (eg osteosarcoma). Tablets are given every 12 hours. With chronic dosing, oral morphine is one third to one half as potent as *i/m* morphine, although at the start of treatment it may only have the potency of one sixth the dose of *i/m* morphine. Adjustment to the dosage should be made not more frequently than every 48 hours to allow equilibration of plasma levels.

- ***Tramadol* (TramalSR (CSL))**

Tramadol is a weak agonist at the μ opioid receptor which also has actions on the GABAergic, noradrenergic and serotonergic receptors. Analgesia produced by tramadol is not completely antagonized by naloxone and the drug is not scheduled as a “controlled drug”. The injectable form of the drug does not appear to offer any particular advantages but the oral formulation is useful in the management of short to medium term pain in dogs and cats at a dose rate of 2 – 4 mg/kg twice a day. Side effects that are occasionally seen include sedation and vomiting. The drug is contraindicated with some antidepressant drugs (including serotonin reuptake inhibitors) but it can be combined safely with non-steroidal anti-inflammatory drugs. It can lower the ictal threshold and therefore should be used with caution in patients with epilepsy.

❖ **Non steroidal anti-inflammatory drugs (NSAIDS)**

NSAID's have long been recognised to be particularly effective for chronic musculoskeletal pain. Newer drugs of this group (eg, firocoxib, meloxicam, carprofen, ketoprofen,) have been shown to be effective against acute pain.

This class of drugs has the potential to cause gastrointestinal ulceration when used for an extended period or if given together with a corticosteroid. Because they may cause renal failure in patients with low blood pressure, some veterinary anaesthetists will not use NSAID's until the patient has recovered from anaesthesia, is normovolaemic and not at risk of further haemorrhage. There is good evidence that NSAID's that selectively antagonise COX 2 isoenzyme of canine cyclooxygenases (firocoxib, meloxicam & carprofen) have less potential to cause gastric or renal damage and as a result these drugs are suitable for long term use.

Meloxicam liquid has been used extensively “off label” for chronic pain in cats. Loading dose of 0.1 mg/kg, followed on days 2 to 5 by 0.05 mg/kg and thereafter 0.05 – 0.1 mg *per cat*.

❖ **The role of tranquillisers in pain control.**

Tranquillisers, when combined with opioid analgesics, appear to either potentiate analgesia or make the pain more tolerable.

Benzodiazepines and acepromazine are useful in this regard. Acepromazine 0.01 mg/kg i/v has proven to be particularly effective.

Some clinical examples

Ovariohysterectomy in a bitch

Premedication: methadone 0.2 – 0.3 mg/kg i/v (+/- acepromazine 0.02 mg/kg) 2 min prior to induction or methadone 0.4-0.5 mg/kg s/c (+/- acepromazine 0.04 mg/kg s/c) 30 min prior to induction

anaesthesia: halothane or isoflurane +/- N₂O. Incremental doses of methadone 0.1 mg/kg i/v

during recovery – incremental methadone (0.1-0.2 mg/kg i/v) if required. Meloxicam 0.2 mg/kg s/c

next 34 hours – one dose of meloxicam to be given 24 hours after the injected dose

Repair of ruptured cranial cruciate ligament

Premedication: methadone 0.2 – 0.3 mg/kg i/v (+/- acepromazine 0.02 mg/kg) 2 min prior to induction or methadone 0.4-0.5 mg/kg s/c (+/- acepromazine 0.04 mg/kg s/c) 30 min prior to induction

anaesthesia: halothane or isoflurane +/- N₂O. Before start of surgery – epidural injection of 0.5% bupivacaine (0.2 ml/kg) with morphine (10 mg/ml) added at 0.1 mg/kg. Patient positioned in dorsal recumbency or in lateral recumbency with injured leg down for 10 minutes prior to the start of surgery. Bolus dose of Hartmanns (20 ml/kg) given i/v during this period.

after closure of the joint: morphine 0.1 mg/kg in one ml of 0.5% bupivacaine given by intrasynovial injection

during recovery : meloxicam 0.2 mg/kg s/c

post operatively: tramadol 2 mg/kg bd for 2 days & meloxicam 0.1 mg/kg po q 24 hrs for 2 weeks, commence course of pentosan polysulphate 48 hours post op. Bandage for 48 hrs post op to minimise swelling.

Hemimandibulectomy

Premedication: methadone 0.2 – 0.3 mg/kg i/v (+/- acepromazine 0.02 mg/kg) 2 min prior to induction or methadone 0.4-0.5 mg/kg s/c (+/- acepromazine 0.04 mg/kg s/c) 30 min prior to induction

Prior to surgery: Bilateral submandibular nerve block with 0.5% bupivacaine

Prior to recovery from anaesthesia: repeat submandibular nerve block, carprofen 4 mg/kg s/c, start i/v infusion of morphine 0.1 mg/kg/hour

Post operative: continue morphine infusion for 12 – 24 hours, carprofen 2 mg/kg bd (s/c or po) for 4 days. Repeat nerve block if needed. When morphine infusion is stopped, start tramadol 2-4 mg/kg bd for 3 days.

Lateral ear canal resection

Premedication: methadone 0.2 – 0.3 mg/kg i/v (+/- acepromazine 0.02 mg/kg) 2 min prior to induction or methadone 0.4-0.5 mg/kg s/c (+/- acepromazine 0.04 mg/kg s/c) 30 min prior to induction

After induction of anaesthesia but prior to surgery: commence morphine infusion at 0.2 mg/kg/hour. Give increments of morphine of 0.1 mg/kg as needed.

Before surgical closure: topical application of bupivacaine 0.5% to the surgical site not exceeding 0.5 ml/kg

prior to recovery from anaesthesia: meloxicam 0.2 mg/kg s/c

post operatively : reduce rate I/V infusion of morphine to 0.1 mg/kg/hour (?). Give I/V increments of morphine 0.1 mg/kg as needed. Give acepromazine 0.01 mg/kg i/v as needed. Continue morphine infusion for 24 hours then start tramadol 2-4 mg/kg po bid for 3 days. Give meloxicam 0.1 mg/kg q 24 hours for one week