ANALGESIA IN EXOTICS: A REVIEW AND UPDATE

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Introduction

Plato, 375 BC, stated that, “Pain is an emotion that dwells in the brain”. In the last century the knowledge of pain physiology and its manipulation developed in leaps and bounds and yet analgesia for animals, especially the exotic species, has only really come into its own in the last 10-20 years.

Analgesia literally translates as “without pain”, Baillière’s Veterinary Dictionary (1995) defines analgesia as an “absence of sensibility to pain, particularly the relief of pain without loss of consciousness; absence of pain or noxious stimulation”. There is only one class of drugs that provide absolute analgesia and these are the local anaesthetics, all other drugs are either hypoalgesics or anti-hyperalgesics and this should be remembered when providing so-called analgesia.

This lecture aims to provide revision on basic analgesic techniques and update on newer agents being used.

Pain physiology and targets for analgesics

Do different taxa feel pain?

If in doubt then YES: anthropomorphism useful tool
• **Invertebrates**
  - Similar neuropeptides found in invertebrates as in higher vertebrates
  - Work on the Sea Hare (*Aplysia californica*) has shown withdrawal reflexes, central sensitisation, and behaviour thought to be attributable to equivalent of fear

• **Fish**
  - Similar receptors, neuropeptides, encephalins, and opioid receptors but unknown whether there is central processing
  - Opioid receptors are present: possible same role or nociception evolved later
  - Clinical improvements seen when using analgesia after noxious stimuli/surgery when compared to animals not having analgesics
  - More developed in teleosts then the elasmobranchs

• **Amphibians**
  - Four distinct afferent fibre populations, one set for thermal stimulation, and others respond to painful stimuli
  - Endogenous opioid system present as in mammals: spinal administration of endogenous opioids generates a dose dependant increase in nociceptive threshold
  - Morphine efficacy in pain tests
  - Opioid receptors mainly kappa type
  - $\alpha_2$ receptors also similar to mammals with similar analgesia properties

• **Reptiles**
  - Similar gross and histological appearance of the spinal cord to mammals
  - Higher concentration of encephalin receptors in the brain of some turtle species than mammals
  - Crocodiles more sensitive to low dose opioids and marked effect on pain trials

• **Avian**
  - Same neural circuitry, neurotransmitters, and neureceptors as mammals
  - Opioid receptors: kappa more common then mu

• **Mammals**
  - Same system as humans in every respect

The question should not be does an animal feel pain, but can an animal’s response to pain be recognised by a clinician?

The physiological effects of pain

• **Cardiovascular**
  - Increased heart rate
  - Increased blood pressure
  - Increased cardiac output
  - Increased risk of arrhythmias
  - Impaired cardiovascular function

• **Respiratory**
  - Increased respiratory rate
  - Reduced ventilation
  - Hypoxaemia
  - Hypercapnia
  - Acidosis
  - Increased risk of atelectasis
  - Increased risk of pneumonia

• **Gastrointestinal**
  - Increased intestinal secretions
o Paralytic ileus
o Vomiting
o Anorexia
o Increased risk of gastric ulceration
o Intestinal pain

• Urinary
  o Urine retention
  o Water and sodium retention
  o Electrolyte changes

• Metabolism
  o Increased metabolism and oxygen consumption
  o Breakdown of fat, muscle, and glucose stores
  o Delayed wound healing
  o Increased tissue breakdown
  o Weight loss

• Immune system
  o Impaired immune system
  o Increased risk of infection and sepsis
  o Enhanced metastatic tumour spread
  o Increased risk of tumour recurrence

• Nervous system
  o Sensitisation of pain pathway
  o Hyperalgesia
  o Allodynia
  o Heightened pain perception and chronic pain

Types of analgesics

Support

• Analgesia does not just have to involve the administration of pharmaceutical agents.
• Observing basic patient care can be more efficacious than most drugs and when combined with an analgesia therapeutic plan they can be synergistic
• Adjuncts to analgesia include;
  o Support: fracture stabilisation, wound dressings, etc
  o Cardiovascular and respiratory support
  o Nutritional support
  o Gentle surgery (use of muscle relaxants)
  o Muscle relaxation e.g. diazepam
  o Sedatives to reduce fear and perception of pain
  o Comfortable environment at suitable POTZ
  o Ensure empty bladder and rectum
  o Gentle physiotherapy
  o Acupuncture
  o TLC

Opioids

• Opiates are drugs derived from the opium poppy (Papaver somniferum) i.e. morphine
• Opioids are any drugs that work in a similar manner to morphine
• Narcotic: any opioid but this refers to the state similar to sedation/euphoria that these drugs produce (“narcosis”)
• Opioid receptors are found in the CNS, gastrointestinal tract and joints, possibly other peripheral sites too e.g. rat vas deferens has its own opioid receptor (ε). They include;
  o OP-1 or δ (delta): analgesia, modulation of µ, and possible antitussive
  o OP-2 or κ (kappa): analgesia, dysphoria, anti-tussive
• OP-3 or μ (mu): analgesia, respiratory depression, narcosis, ?addiction

• Opioid effects include:
  o Analgesia
  o Respiratory depression (reduction in sensitivity to CO₂)
  o Gastro-intestinal effects: vomit (CTZ: outside blood brain barrier), anti emetic (vomit centre: inside blood brain centre), [interestingly, the more fat soluble the opioid the easier it is to cross the blood brain barrier and this means the animal is less likely to vomit e.g. methadone compared to morphine], increased gut motility but this is uncoordinated and therefore peristalsis is decreased overall)
  o Cardiovascular effects: variable depending on the drug and the species. Some opioids cause histamine release and hypotension. Morphine acts centrally to create hypotension and bradycardia. Etorphine and Carfentanil can cause a massive hypertension

• The receptors have variable effects on the body systems;

<table>
<thead>
<tr>
<th>Opioid receptor</th>
<th>µ</th>
<th>κ</th>
<th>δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesia</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Supraspinal</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Spinal</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>• Peripheral</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Resp depression</td>
<td>+++</td>
<td>?</td>
<td>++?</td>
</tr>
<tr>
<td>Pupil</td>
<td>Variable on species</td>
<td>Miosis</td>
<td>Mydriasis</td>
</tr>
<tr>
<td>GI motility</td>
<td>↓↓</td>
<td>↓?</td>
<td>↓↓</td>
</tr>
<tr>
<td>Euphoria</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dysphoria</td>
<td>-</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Sedation</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Dependence</td>
<td>+++</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

• Receptor affinity and potency are not the same, an opioid may have a high affinity but the effect may be agonistic or antagonistic:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Opioid receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>µ</td>
</tr>
<tr>
<td>Pethidine (meperidine)</td>
<td>++</td>
</tr>
<tr>
<td>Morphine</td>
<td>+++</td>
</tr>
<tr>
<td>Methadone</td>
<td>+++</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>+++</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>+++</td>
</tr>
<tr>
<td>Etorphine</td>
<td>+++</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>+++ (partial ag)</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>++(ag/antag)</td>
</tr>
<tr>
<td>Naloxone</td>
<td>+++(antag)</td>
</tr>
</tbody>
</table>

• Opioids are metabolised in the liver with excretion in the bile and the urine: can lead to enterohepatic recycling if active metabolites e.g. etorphine. Faster metabolism in ruminants generally

• Routes
  o Oral: Most species see first pass metabolism, therefore not recommended
  o SC: Well absorbed
  o IM: Well absorbed
  o IV: Reduce dose, risk of histamine release and exacerbate side effects
  o Rectal: well absorbed
  o Transdermal: lipophilic opioids such as fentanyl only
  o Intrathecal: useful direct effect on the spine
Corticosteroids

- Most effective anti-inflammatory drugs
- Not true analgesic: very efficacious at reducing inflammation and associated soup of noxious chemicals that has an analgesic effect i.e. indirect analgesia
- Anti-inflammatory action mediated through intracellular inhibition of phospholipase A2 (PLA2): this enzyme is the primary enzyme involved in the cascade of cell membrane phospholipids degradation to inflammatory mediators. Blocking or reducing the effect of PLA2 results in:
  - Reduction in COX-2 products
  - Reduction in prostaglandins
  - Reduction in prostacyclins
  - Reduction in thromboxanes
  - Reduction in leukotrienes
  - Reduction in platelet activating factor
  - Reduction in nitric oxide
  - Membrane stabilising effects
- Side effects are numerous
  - Immunosuppression
  - Hypothalamic-pituitary-adrenal axis suppression
  - Contraindicated in corneal ulceration
  - Laminitis in susceptible animals
  - Care in pregnant animals
- Mentioned for completeness but not recommended as a primary analgesic due to side effects

Non-steroidal anti-inflammatory drugs (NSAIDs)

- NSAIDs are any anti-inflammatory agents that are not a steroid
- NSAIDs inhibit cyclooxygenase (COX) enzymes. COX enzymes convert arachidonic acid into thromboxanes and prostaglandins/prostacyclins: one half of the pathway inhibited by steroids
- There are two isoforms of COX: COX-1 and COX-2;
  - COX-1: normal housekeeping enzyme used in many protective roles and its inhibition is associated with many of the side effects
  - COX-2: induced in inflamed tissues
  - However not that simple: COX-2 important in angiogenesis of wound healing, housekeeping in the kidney, and is found in the CNS. And COX-1 also has the ability to produce inflammatory products. The ideal COX inhibitor is COX-2 selective, not specific.
- Properties include;
  - Anti-inflammatory
  - Chemotactic (NSAIDs do not block leukotrienes as steroids do)
  - Analgesic: prevent prostaglandin sensitisation locally and peripherally
  - Anti-pyretic: reduction in pyrogens and therefore fever
- Side effects
  - Gastrointestinal ulceration
  - Renal medullary/papillary necrosis: acute renal failure
  - Hepatotoxicity (especially paracetamol)
  - Embryotoxicity: especially aspirin, especially first trimester
  - Bone marrow toxicity
  - Delayed parturition
  - Worsen bronchoconstriction in asthmatics
  - Chondrodestructive e.g. phenylbutazone, however carprofen and meloxicam are chondroprotective at low doses
- Metabolism mainly in the liver, variable between species: cats cannot glucuronidate NSAIDs very well and care should be taken in these species
• Routes:
  o Oral: well absorbed
  o SC: well absorbed
  o IM: well absorbed but not needed
  o IV: takes just as long as SC injection before clinical effect

**Local anaesthetics**
- Local anaesthetics reversibly block voltage-gated sodium channels and therefore prevent membrane depolarisation which blocks transmission: only true analgesic
- Unmyelinated nerves are preferentially blocked over myelinated nerves
- Inactivated channels are preferentially blocked before open or resting channels: a voltage gate exists in one of three states: resting > open > inactivated > resting
- This results in a mixture of some myelinated fibres becoming blocked before unmyelinated if they have a higher firing rate then slower unmyelinated nerves. In general;
  o Preganglionic sympathetic (poorly myelinated) first
  o Postganglionic sympathetic (mix unmyelinated and myelinated): pain and temperature
  o Touch, deep pressure and muscle spindles (myelinated)
  o Motor fibres to muscle spindles (myelinated)
  o Proprioception and somatic fibres (myelinated)
- Differential nerve blockade can occur due to different rate of blockade: results in a mantle effect and can be seen where proximal limb will become desensitised before the distal, reversal is *vice versa*.

<table>
<thead>
<tr>
<th>Drug</th>
<th>pKa</th>
<th>Onset</th>
<th>Rel lipid solubility</th>
<th>Toxicity</th>
<th>Potency</th>
<th>Protein binding</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procaine</td>
<td>8.9</td>
<td>Slow</td>
<td>1</td>
<td>Very low</td>
<td>Medium</td>
<td>6%</td>
<td>Short</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>7.7</td>
<td>Fast</td>
<td>5</td>
<td>Medium</td>
<td>Medium</td>
<td>65%</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>7.7</td>
<td>Fastish</td>
<td>1.5</td>
<td>Low</td>
<td>Medium</td>
<td>55%</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Mepivicaine</td>
<td>7.6</td>
<td>Fast</td>
<td>1.7</td>
<td>Low</td>
<td>Medium</td>
<td>75%</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Bupivicaine</td>
<td>8.1</td>
<td>Slow</td>
<td>48.5</td>
<td>High</td>
<td>High</td>
<td>95%</td>
<td>Long</td>
</tr>
</tbody>
</table>

- The dissociation constant (pKa) determines onset (inflamed tissue more acidic): warming solution reduces the pKa and hastens onset (and reduces pain of injection)
- Lipid solubility determines potency
- Protein binding determines duration
- Local anaesthetics also have vasodilation/vasoconstriction properties of their own: affects duration. It is common for local anaesthetics to have vasoconstrictors added (e.g. adrenalin): this is used to prolong the length of blockade by reducing blood flow local to the local anaesthetic and therefore reduce systemic absorption: pH change by adding adrenalin actually decreases the pH and favours the ionised form of the local delaying onset (but offset by higher concentrations of local anaesthetic by the vasoconstriction with negligible clinical effect)
- Toxic doses may be species dependent but in general:
  - Lidocaine 4-6mg/kg
  - Bupivicaine 1-2mg/kg
- Toxic effects include:
  - True allergic reactions
  - Local tissue injury/neurotoxicity: preservatives, vasoconstriction, iatrogenic needle stick
  - Systemic toxicity: mainly brain and heart excitable cells become stabilised and prevents normal conductance: depressed consciousness, seizures, coma, respiratory arrest, and CNS depression.
  - These can occur secondary to absolute overdose, inadvertent intravascular injection, or individual species sensitivity
Routes include:
- Topical: mucous membranes, corneal, dermal, intra-articular, intrapleural, intrabdominal and splash blocks to wounds
- Non specific infiltration: line block, inverse L block, ring block, and field block
- Specific nerve blocks: target specific nerve that supplies field of surgery or irritation
- Intravenous regional block (IVRA)

\(\alpha_2\) adrenoceptor agonists
- CNS analgesic effects
- \(\alpha_2\) receptors are found in close association with opioid receptors in locations of the CNS involved with pain pathways which may explain the synergistic effects seen when these two drugs are administered together
- Many side effects: sedatives, cardiovascular and respiratory side effects and therefore not used as primary analgesic agents very often
- Useful in low dose infusions
- Possibility that \(\alpha_2\) antagonists may partially reverse the effect of opioids

Ketamine
- Glutamate is an important excitatory neurotransmitter in the CNS: it binds to NMDA receptors (and three other receptors)
- Ketamine is an NMDA antagonist but also has some opioid actions too: it is antagonistic at \(\mu\) receptors but agonistic at \(\kappa\) and \(\delta\) receptors
- Ketamine also stimulates the sympathetic system
- As an analgesic ketamine is administered in very small doses (approximately 1/10\(^{th}\) of induction doses) or by infusions e.g. 0.01-0.02mg/kg/min
- Can also be administered as an epidural

Nitrous oxide
- Analgesic properties: thought to act as an NMDA antagonist but also stimulates endogenous opioid production
- Very useful in combination as part of balanced anaesthesia and analgesia: also reduces the requirements for other anaesthetic agents with no cardiovascular or respiratory effects
- Care: second gas effect and diffusion hypoxia
- Care: gas filled structure inflation

Anti-convulsants
- Gabapentin and pregabalin
- GABA analogues that modulate the actions of voltage-gated calcium channels which are commonly up-regulated in chronic pain
- Useful in neuropathic pain (pain from damaged neuronal tissue e.g. amputations)

Other novel analgesics are becoming available and seem to have promising clinical effects. These include:
- Tetrodotoxin antagonists
- Cannabinoids
- Cholecystokinin antagonists
- Resiniferatoxin (Capsaicin)
- Tricyclic antidepressants

The following pages provide doses for the commonly used analgesic agents across the taxa. Invertebrates have not been included as analgesic use is anecdotal if at all.
### Fish, amphibian, reptilian and avian analgesia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Fish</th>
<th>Amphibian</th>
<th>Reptile</th>
<th>Avian</th>
<th>Route/ comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td>-</td>
<td>49mg/kg SC</td>
<td>5-10 mg/kg IM no effect snakes</td>
<td>1-4mg/kg</td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>-</td>
<td>38-42mg/kg</td>
<td>0.5-4mg/kg intracoloemic</td>
<td>2.5-3mg IM, SC</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>-</td>
<td>-</td>
<td>2.5-3mg IM, SC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>-</td>
<td>0.5mg/kg SC</td>
<td>-</td>
<td>0.2mg/kg</td>
<td>SC</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>-</td>
<td>38mg/kg SC</td>
<td>0.005-0.02-1mg/kg IM every 24-48hr</td>
<td>0.1-0.5mg/kg</td>
<td></td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.05-0.1mg/kg IM</td>
<td>0.2-0.4mg/kg IM</td>
<td>0.4-1.5mg/kg IM higher doses sedation</td>
<td>0.05-0.75-4mg/kg IM</td>
<td></td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carprofen</td>
<td>-</td>
<td>-</td>
<td>1-4mg/kg first then half dose every 24 hours</td>
<td>2-4mg/kg bid-tid</td>
<td>PO, SC, IM, IV</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>-</td>
<td>-</td>
<td>0.1-0.2mg/kg PO every 24 hours</td>
<td>0.2mg/kg IM, IV</td>
<td>0.1mg/kg sid</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>-</td>
<td>-</td>
<td>2mg/kg every 24 hours</td>
<td>2mg/kg sid-tid</td>
<td></td>
</tr>
<tr>
<td>Tepoxalin</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Flunixin</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td><strong>Local anaesthesia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lignocaine</td>
<td>Do not exceed 1-2mg/kg</td>
<td>Local infiltration: care with topical absorption</td>
<td>Infiltrate to effect</td>
<td>Infiltrate to effect</td>
<td>Toxic dose: 4-6mg/kg</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>-</td>
<td>As for lignocaine</td>
<td>As for lignocaine</td>
<td>Up to 10mg/kg in birds</td>
<td>Toxic dose: 1-2mg/kg</td>
</tr>
</tbody>
</table>
**Canine, feline, bovine, equine and porcine analgesia**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Canine</th>
<th>Feline</th>
<th>Bovine</th>
<th>Equine</th>
<th>Porcine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td>2-10mg/kg IM</td>
<td>5-10mg/kg IM</td>
<td>2mg/kg IM</td>
<td>2mg/kg</td>
<td>2mg/kg IM</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.25-2mg/kg IV/IM</td>
<td>0.1-0.5mg/kg IM/SC</td>
<td>Not recommended</td>
<td>0.1-0.2mg/kg IM/IV</td>
<td>0.2mg/kg IM</td>
</tr>
<tr>
<td>Methadone</td>
<td>0.1-0.4mg/kg IM/IV/SC</td>
<td>0.1-0.2mg/kg IM/IV/SC</td>
<td>-</td>
<td>0.1-0.5mg/kg IM/IV</td>
<td>-</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.001-0.005mg/kg IV</td>
<td>0.001-0.005mg/kg IV</td>
<td>-</td>
<td>-</td>
<td>0.2mg/kg intraop</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.006-0.02mg/kg IV/IM</td>
<td>0.006-0.02mg/kg IV/IM</td>
<td>-</td>
<td>-</td>
<td>0.006-0.02mg/kg IV/IM</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.05-0.6mg/kg IM/IV</td>
<td>0.05-0.6mg/kg IM</td>
<td>0.005mg/kg IM</td>
<td>0.05-0.2mg/kg IM/IM/SC</td>
<td>0.1mg/kg IM</td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carprofen</td>
<td>4mg/kg first then 2mg/kg bid</td>
<td>4mg/kg first then 2mg/kg bid</td>
<td>1.4mg/kg single dose</td>
<td>0.7mg/kg IV/PO sid</td>
<td>-</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>0.2mg/kg PO/SC then 0.1mg/kg sid PO</td>
<td>0.3mg/kg SC/PO then 0.1mg/kg sid for 4 days</td>
<td>0.5mg/kg single dose</td>
<td>0.6mg/kg PO/IV</td>
<td>-</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>2mg/kg sid up to 3 days</td>
<td>2mg/kg sid up to 3 days</td>
<td>3mg/kg IM/IV 3 days</td>
<td>2.2mg/kg IV</td>
<td>-</td>
</tr>
<tr>
<td>Tepoxalin</td>
<td>10mg/kg PO sid</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aspirin</td>
<td>10mg/kg PO bid</td>
<td>10mg/kg eod PO</td>
<td>100mg/kg PO bid</td>
<td>100mg/kg PO tid</td>
<td>10mg/kg PO</td>
</tr>
<tr>
<td>Paracetemol</td>
<td>25mg/kg qid PO</td>
<td>Contraindicated</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Phenylbutazone</td>
<td>2-20mg/kg bid</td>
<td>6-8mg/kg bid</td>
<td>-</td>
<td>4.4mg/kg IV, then half for 2-5 days bid</td>
<td>-</td>
</tr>
<tr>
<td>Flunixin</td>
<td>1mg/kg IV/IM 3 days</td>
<td>1.1mg/kg single dose</td>
<td>1mg/kg IM</td>
<td>1.1mg/kg IV/IM sid</td>
<td>1mg/kg IV/IM</td>
</tr>
<tr>
<td><strong>Local anaesthesia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lignocaine</td>
<td>Infiltrate to effect</td>
<td>Infiltrate to effect</td>
<td>Infiltrate to effect</td>
<td>Infiltrate to effect</td>
<td>Toxic dose: 4.6mg/kg</td>
</tr>
<tr>
<td>Bupivicaine</td>
<td>Infiltrate to effect</td>
<td>Infiltrate to effect</td>
<td>As for lignocaine</td>
<td>Infiltrate to effect</td>
<td>Toxic dose: 1-2mg/kg</td>
</tr>
</tbody>
</table>
## Lagomorphs, rodents, ferrets, and primates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rabbit</th>
<th>Guinea pig</th>
<th>Chinchilla</th>
<th>Mouse</th>
<th>Ferrets</th>
<th>Primates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td>5-10mg/kg q2-3hr</td>
<td>10mg/kg q2-4hr</td>
<td>10-20mg/kg q6hr</td>
<td>20mg/kg q2-3hr</td>
<td>5-10mg/kg q2-4hr</td>
<td>2-4mg/kg q3-4hrs</td>
</tr>
<tr>
<td>Morphine</td>
<td>2-5mg/kg q2-4hr</td>
<td>2-5mg/kg q2-4hr</td>
<td>2-5mg/kg q4hr</td>
<td>5-5mg/kg q2-6hr</td>
<td>1-2mg/kg PO/SC/IM/IV q4hrs</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.01-0.05mg/kg q6-12hr</td>
<td>0.05mg/kg q8-12hr</td>
<td>0.05-2.5mg/kg q6-12hr</td>
<td>0.01-0.03mg/kg q8-12hr</td>
<td>0.005-0.03mg/kg q6-12hrs</td>
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<tr>
<td>Butorphanol</td>
<td>0.1-0.5mg/kg q2-4hr</td>
<td>2mg/kg q2-4hr</td>
<td>0.2mg/kg q4hr</td>
<td>1-5mg/kg q2-4hr</td>
<td>0.05-0.5mg/kg q8-12hr</td>
<td>0.01-0.02mg/kg q3-4hr Care: +++ resp depression</td>
</tr>
</tbody>
</table>

**NSAIDs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rabbit</th>
<th>Guinea pig</th>
<th>Chinchilla</th>
<th>Mouse</th>
<th>Ferrets</th>
<th>Primates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carprofen</td>
<td>4mg/kg SC sid</td>
<td>1.5mg/kg bid PO</td>
<td>1-4mg/kg PO/SC sid</td>
<td>4mg/kg PO/SC sid</td>
<td>5mg/kg PO/SC sid</td>
<td>1mg/kg PO bid/sid</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>0.2mg/kg PO/SC sid</td>
<td>0.1-0.2mg/kg PO/SC sid</td>
<td>0.1-0.2mg/kg PO/SC sid</td>
<td>0.1-0.2mg/kg PO/SC sid</td>
<td>0.1-0.2mg/kg PO/SC sid</td>
<td>-</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>1mg/kg IM/SC sid</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5mg/kg IM q6-8hrs</td>
</tr>
<tr>
<td>Aspirin</td>
<td>10-100mg/kg PO q4hr</td>
<td>80-100mg/kg PO q4hr</td>
<td>100-200mg/kg PO q6-8hr</td>
<td>100-150mg/kg PO q4hr</td>
<td>0.5-22mg/kg PO q8-24hr</td>
<td>5-10mg/kg PO q4-6hrs</td>
</tr>
<tr>
<td>Flunixin</td>
<td>1-2mg/kg SC bid/sid</td>
<td>2.5-5mg/kg SC q6-12hr</td>
<td>2.5mg/kg SC q12-24hr</td>
<td>2.5mg/kg SC q12-24hr</td>
<td>0.3-0.5mg/kg PO/SC/IV bid/sid</td>
<td>0.3-1mg/kg IV/SC bid/sid</td>
</tr>
</tbody>
</table>

**References**


Fubini, S.L. and N.G. Ducharme, *Farm Animal Surgery*. 2004, St. Louis: Saunders. 607


