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Opioids are undeniably the drugs of choice for managing moderate to severe pain in dogs and cats. They reduce the conscious sensation of pain and in humans reduce the anxiety associated with severe pain. Studies also suggest that opioids may mediate analgesia locally within damaged tissue.

The majority of opioids in clinical use are synthesized from morphine and are termed semi-synthetic. Lipid solubility is variable and impacts proportionally on duration of effect. Almost all opioids undergo hepatic metabolism, some with active metabolites.

Injection is the most common route of administration, although pethidine and (to a lesser extent) morphine may cause histamine release and arterial hypotension when given in this way.

All opioid effects are mediated by activity at opioid receptors: mu, kappa, delta and (more recently) orphan. Receptors differ in their function, binding and distribution. Drugs are classed as agonists, partial agonists, mixed agonist-antagonists and pure antagonists.

Opioids are effective at controlling the intensity of most types of pain depending on dose given. Sensitivity to touch, pressure & mechanical stimulation are relatively unaffected. Considerable inter-individual variation exists in opioid requirements in humans; this has in part a genetic basis (eg red-haired individuals have greater sensitivity), and is true in dogs and cats. All receptors mediate analgesia at spinal and supra-spinal levels; mu agonists are the most clinically effective analgesics. Other CNS effects include euphoria (an effect of mu agonists and partial agonists) and dysphoria, which can be moderated by prior or co-administration of a sedative such as acepromazine.

Of major importance to the intensivist and emergency clinician are the effects on cardiovascular and respiratory function. Cardiovascular effects depend on the drug, species and route of administration. Centrally-mediated bradycardia may occur but is not usually clinically significant in patients already in pain or unless the potent opioids such as fentanyl and its derivatives are given intravenously. Any bradycardic effects in cats are more likely to result from an indirect calming effect. Hypotension may result from bradycardia and may also occur following rapid intravenous administration of morphine and pethidine (much more severely with the latter), probably as a result of histamine release.

Respiratory depression occurs as a result of reduced sensitivity of the respiratory centre to carbon dioxide. In contrast to humans, clinically significant respiratory depression is extremely uncommon unless potent opioids are used intra-operatively. Hypoventilation as a result of chest pain may be improved by opioid analgesia. Patients with hypoventilation following head injury may be at risk of intracranial hypertension (which develops as a result of carbon dioxide-induced cerebral vasodilation) due to exacerbation of respiratory depression by opioids. Severely obtunded or comatose patients should probably not receive opioids until ventilation and/or intracranial pressure are controlled.

Gastrointestinal effects include vomiting & defecation in pain-free dogs; effects are lessened if the patient is already in pain. Vomiting is less after slow iv injection than im injection. Much controversy exists over the clinical use of opioids in the management of pancreatic pain. Experimental studies have documented increases in ductal pressure associated with the administration of morphine, methadone, fentanyl, and also pethidine, a drug always credited with spasmolytic properties. However, the clinical significance of this effect is not clear and the author is not aware of any clinical studies in animals that demonstrate exacerbation of pancreatitis following administration of these drugs. If the clinician is concerned then the use of buprenorphine may be preferred due to its minimal effect on ductal pressure; alternatively opioids may be given epidurally or other agents (eg ketamine) considered.

**Morphine**

Morphine is a powerful analgesic, which despite its lack of a veterinary licence is widely utilised due to its considerable efficacy and reliability. Systemic administration at doses of 0.1-0.4 mg/kg SC or IM produces analgesia of 4 hours duration. The duration of effect probably depends on level of painful stimulus and dose. Morphine is also effective orally (despite significant first-pass metabolism) and rectally. Onset of action is usually 5-10 minutes even after IV injection. Analgesia is dose-dependent; in severe pain in dogs the author has used morphine at doses of up to 4-5mg/kg, titrated slowly up to a desired clinical effect. The poor lipid solubility of morphine makes it suitable for prolonged analgesia when used epidurally as the preservative free preparation at 0.1 mg/kg. Cats do not metabolise morphine as rapidly as dogs and a dosing interval of...
4-6 hours is probably appropriate in this species. Vomiting seen after the use of morphine for premedication in healthy patients is much less common in critically patients in pain.

**Methadone**

Methadone is a synthetic opioid mu-agonist but also has NMDA receptor antagonist activity, and is used in the management of acute & chronic neuropathic pain. The long half-life observed in humans does not appear to be replicated in dogs or cats. Duration of effect using doses of 0.1-0.5mg/kg is approximately 4-5 hours.

**Pethidine**

Pethidine is the only mu-receptor agonist licensed as a sole agent for veterinary use in the UK. It is less potent than morphine but onset of action is rapid, making it a useful drug for acute use in trauma. Duration of action is short (60-120 minutes depending somewhat on dose). Pethidine does not tend to cause vomiting with routine use.

**Fentanyl**

A very potent agonist, approximately 50 times more effective than morphine but with a rapid onset and short duration. Used primarily for intraoperative analgesia as part of a balanced anaesthetic. Normal doses (5-20microg/kg) produce profound respiratory depression or apnoea in anaesthetised patients; provision for IPPV must therefore be available. Short action mainly due to redistribution rather than elimination therefore risk of cumulation or prolonged respiratory depressant effects. Large doses may produce a profound bradycardia.

Fentanyl is also available in a transdermal patch form (Durogesic®; Janssen) intended for use in human patients suffering from chronic pain. Onset of analgesia is slow (up to 12 hours) but the patches can provide effective pain relief for up to 72 hours. All CD II regulations still apply.

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Dose</th>
<th>Total drug content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Dogs (&lt;5kg) &amp; Cats</td>
<td>25 mcg/hr</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Dogs: 5-10 kg</td>
<td>25 mcg/hr</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Dogs: 10-20 kg</td>
<td>50 mcg/hr</td>
<td>5 mg</td>
</tr>
<tr>
<td>Dogs: 20-30 kg</td>
<td>75mcg/hr</td>
<td>7.5 mg</td>
</tr>
<tr>
<td>Dogs: &gt;30 mg</td>
<td>100 mcg/hr</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

Small dogs and cats may be dosed with 1/2 patch, but the patch should not be cut in half. Cover 1/2 the gel membrane with tape. "Half-patch dosing" is suggested for pediatric, geriatric and systemically ill cats and small dogs.

The patch may be placed either on the dorsal or lateral cervical area or the lateral thorax. If the neck is used, collars/leashes cannot be placed over the patch. The thorax is easily used and contact maximized (especially in cats), but can be difficult to bandage. The site must be clean and dry at the time of application. Do not place where a heating pad may come into contact as this may increase release of drug from the patch. The site should be closely clipped with at least a 1 cm margin around the patch. Do not shave as cuts, abrasions or wounds can alter drug absorption. After clipping, wipe with a damp swab to remove small hairs and skin debris; do not scrub or surgically prepare the site. Allow to completely dry before application.

Remove the occlusive membrane from the patch. Be careful not to expose your skin to the gel surface. Place the patch over the clipped area and hold it in place for 2-3 minutes to ensure adherence. Dispose of used patches in a safe and effective manner and record disposal date and method. All patients wearing patches should have heart and respiratory rates monitored regularly.

**Buprenorphine**

Buprenorphine is classified as a partial agonist at mu opioid receptors, although partial agonist effects are probably not significant at doses currently used clinically (20-40 microg/kg q6-8h). The drug has a slow onset of action (30-40 minutes for maximal receptor binding), which limits its usefulness in the acute setting, but duration of analgesia is good (6-8h) and analgesic potency in cats is comparable with that of morphine. Injectable buprenorphine can be administered orally in cats to provide analgesia at similar doses to those used parenterally.

**Butorphanol**

Butorphanol is a mu-receptor antagonist but a kappa-agonist. It possesses excellent sedative properties, particularly as part of a neuroleptanalgesic combination, but its analgesic benefits are controversial and the author cannot currently recommend the drug for use as a "front-line" analgesic. Its effects are short in duration (>90minutes). Butorphanol provides better visceral analgesia than somatic analgesia and its use should probably be limited to patients with acute visceral pain (enteritis, cystitis).
Referencias