Review Article

REVIEW ON THERAPEUTIC MANAGEMENT OF PAIN IN ANIMALS

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ABSTRACT

Animal pain management is an important aspect in veterinary medicine. Trauma, illness and surgery can all result in acute pain and good management of pain is required for animal welfare (i.e., Health, physical and mental wellbeing). Newer classes of drugs are emerging for the management of pain which has lesser side effects and more efficacy than older drugs which were used against pain. Combination of two or more drugs has been proved to be more effective for the management of pain than the single drug usage. Selection of the most suitable drug combination is based on the severity of pain, effectiveness of the drug and also health status of the animal. Management of animals that are under pain needs a combination of good nursing, nondrug therapies (for example, ice packs or heat, bandaging and physical therapy) and drug treatments. The article reviews about the classes of drugs which are used for the management of acute and chronic pain in animals, their most common side effects, and the treatment regimen for different class of drugs. It is aimed to guide the veterinary practitioner to select and dose the animals with effective analgesics for the management of pain.

Keywords: Analgesics, Animal welfare, NSAIDs, Opioids, Pain management

Received : 04.01.2022 Revised : 18.03.2022 Accepted : 12.04.2022

INTRODUCTION

Pain is defined as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Valverde and Gunkel, 2005). Therapy for the pain generally involves pharmacological agents like opioids, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, local anesthetics, antihistaminics, α_2-agonists, ketamine and gabapentin etc., and non therapeutic approaches like acupuncture, physiotherapy etc. Concurrent use of more than one type of analgesic agent, may be more effective for pain relief than the

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use of any single drug type and may allow the dose of each individual drug to be reduced. The most commonly used classes of pain-relieving therapeutic agents in domestic animals are opioids (narcotic analgesics) and NSAIDs (non-narcotic analgesics) (Vinuela-Fernandez *et al.*, 2007).

Opioids

Opioids are the most powerful pain-relieving compounds available for the systemic treatment of acute pain in many species of animals. Opioids act as agonists, antagonists, partial agonists and mixed agonist/antagonists to four types of opioid receptors (Mu, Kappa, Delta and Sigma), with multiple receptor subtypes. Opioids combine reversibly with specific receptors in the brain, spinal cord, and periphery, altering the transmission and perception of pain. In addition to analgesia, opioids can induce other CNS effects that include sedation, euphoria, dysphoria, and excitement (Sneddon *et al.*, 2014).

The important opioid (opiates: synthetic/semisynthetic) analgesics are morphine, oxymorphone, butorphanol, codeine, nalorphine, levallorphan, pethidine, fentanyl, methadone, dextropropoxyphene, pentazocine, cyclazocine, etorphine, buprenorphine, mepiridine (pethidine), sufentanil, methadone, alfentanil, carfentanil, remifentanyl, nalbuphine, tramadol hydrochloride etc. (Pathan and Williams, 2012).

Characteristic features:

- Considerable variation between species and among the different opioids with regard to the effects of opioids.
- Use should be reserved for pain that will not respond to other medications or when pets are in terminal condition.
- Also, with time, doses have to be increased to obtain comparable pain relief
- Schedule II drugs, with potential abuse liability. Hence the owners need to be informed about their ill effects in humans before prescribing and using these agents, the doctor who prescribes must carefully maintain all the records pertaining to the case to avoid any complications (Kaye *et al.*, 2017).

Central effects: analgesia, reduced nociception, euphoria (or dysphoria), elevated mood, relief of the anxiety associated with pain (excessive sedation), respiratory depression, antitussive (cough suppression) effect, bradycardia, hypotension, nausea, vomition, pica and pupillary constriction (Vallejo *et al.*, 2004).

Peripheral effects: reduced propulsive motility of the GIT, increase in sphincter tone resulting in constipation (hence given in combination with laxative), urinary retention, and histamine release (anaphylactoid reaction causing itching or more severe allergic reactions including bronchoconstriction).

- The administration of NSAIDS concomitantly with opioids may allow the effective use of lower doses of opioids with fewer side effects and adequate pain management.

- Generally, produce hyperactivity in ruminants, and particularly chewing behaviour. Doses of opiates required for immobilization may vary considerably between ruminant species and in general the dose rate (mg/kg) required increases as the size of the animal decreases.
- They should be used with care in acutely uremic and toxemic dogs. It has been recommended to administer half of the usual adult dose of opioids to puppies and kittens. Starting at lower doses and increasing to effect is recommended for analgesia.

Indications: Acute/chronic moderate to severe visceral pain, either preoperatively particularly before orthopedic surgery or to reduce pain due to trauma or after surgery. They are used in horses for various ailments, particularly to relieve acute pain of spasmodic colic. They are also combined with suitable tranquillizer as part of of neurolept analgesia for the restraint of animals, and also to provide analgesia as part of a balanced anaesthetic technique (Simon and Steagall, 2017).

Opioids are contraindicated in

- Head injury and raised intracranial pressure, hepatic and renal insufficiency, convulsant states, biliary colic, decreased respiratory reserve as in conditions like emphysema and asthma.
- Strychnine poisoning, tetanus and epilepsy.
- Traumatic shock situations due to their immediate hypotensive effect (Hammond *et al.*, 2008).

Tramadol hydrochloride is a centrally acting analgesic with opioid, monoaminergic, (monoamine reuptake inhibitor) and local anesthetic effects. It has been approved for acute or chronic mild to moderate pain relief in dogs and cats.

- May be combined with other classes of analgesics including steroids, NSAIDs, NMDA antagonists, and gabapentin to allow a lower dose of both drugs to be used.
- Should not be combined with group of drugs like tricyclic antidepressants (TCA; e.g.: clomipramine), selective serotonin reuptake inhibitors (SSRIs; e.g.: fluoxetine) or monoamine oxidase inhibitors (MAOI; e.g. selegiline) due to the risk of serotonin syndrome.
- Rare side effects may include GI disturbances, nausea, pupillary constriction, bradycardia, cough suppression, panting, constipation and sedation, which needs reduction in dosage.
- Not a controlled substance and can be used for pain control in lactating bitches as it is not excreted in milk. It should be used cautiously in animals with a history of seizures as itself can induce seizures (Souza and Cox, 2011).

Non-steroidal anti-inflammatory drugs (NSAIDS)

NSAIDs are the most widely prescribed drugs in the treatment of pain and inflammation in many conditions. NSAID have the potential to relieve pain and inflammation without the immunosuppressive and metabolic side effects associated with corticosteroids. The analgesic, antipyretic and anti-inflammatory effects of NSAIDs associated with properties like being devoid of sedation, hypotension, bradycardia and respiratory depression makes them advantageous over opioids, though with lesser analgesic potency. As with the opioids, different animals react differently to NSAIDs (Mathews, 2000).

Mechanism of action: Act by inhibition of cyclo-oxygenase (COX) enzyme(s) which leads to a decrease in the synthesis of various prostaglandins and thromboxanes. Some may also inhibit phospholipase 'A' enzyme; major mechanism for effects of glucocorticoids on prostaglandin production.

Most of the NSAIDs (aspirin, being the prototype) are nonselective COX inhibitors, with COX 1 inhibition ratio being highest. Meloxicam, nimesulide, etodolac and aceclofenac are considered as preferential COX-2 inhibitors. The newer 'Coxib' class of selective COX-2 inhibitors includes rofecoxib, celecoxib, valdecoxib, parecoxib, deracoxicb, etoricoxib, firocoxib, lumiracoxib etc. are thought to inhibit COX-2 selectively. Paracetamol (acetaminophen) is a selective COX-3 inhibitor with only analgesic and antipyretic actions, devoid of/with minimal anti-inflammatory action (Vane and Botting, 1998).

Pharmacological effects: All NSAID, except for acetaminophen exhibit antipyretic, analgesic, and anti-inflammatory properties. In general, NSAID provide only symptomatic relief from pain and inflammation and do not significantly alter the course of pathologic damage. As analgesics, they are generally less potent than opioids and are therefore more effective against mild to moderate pain.

Indications: NSAIDs are primarily indicated for pain resulting from musculoskeletal injury either due to trauma (or surgery) and to reduce or relieve abdominal pain due to their analgesic, anti-inflammatory and antipyretic action. They are also used as adjunctive therapy to antimicrobial treatment in mastitis, metritis and in acute respiratory diseases in cattle (Mathews, 2000).

Adverse effects: 1) Cellulitis, thrombophlebitis and tissue necrosis with intramuscular or perivascular injections 2) Gastric ulceration by inhibiting the production of PGE and PGI_2. The only exception would appear to be paracetamol as it does not inhibit peripheral oxygenase. The ulcerogenic potential of NSAIDs in any species is increased by concurrent corticosteroid treatment, dehydration, hypovolemic shock and disruption to normal gut blood flow (empty stomach). Agents such as H_2 receptor antagonists (eg: ranitidine), proton pump inhibitors (e.g. omeprazole) or cytoprotective drugs (e.g. misoprostol, sucralfate) are administered to prevent/heal the gastric ulceration effect of NSAIDs. 3) Renal toxicity as a result of reduced renal blood flow and glomerular filtration rate secondary to inhibition of synthesis of renal prostaglandins, that are involved in maintaining renal blood

flow via their vasodilatory actions (Lazzaroni and Porro, 2004).

NSAIDS in cats: The use of paracetamol is contraindicated as the products of its metabolism are extremely toxic. Meloxicam, ketoprofen, carprofen, robenacoxib, flunixin, piroxicam and tepoxalin are effective and well-tolerated analgesics in cats when administered for short-term treatment (three days). However, they should be avoided in: older animals; prior to any surgery where the risk of hypotension is greater than usual (e.g. intestinal); when alpha-2 agonists such as medetomidine are used for sedation or anesthesia. Use of synthetic opioids such as buprenorphine, butorphanol or pethidine provide equally effective analgesia as NSAIDs without the risk of renal toxicity related to reduced renal perfusion (Robertson and Taylor, 2004).

NSAID therapy to be discontinued if animals show any of these signs:

- decrease or increase in appetite or thirst,
- vomiting, diarrhoea or black tarry or bloody stools
- seizure, aggression or confusion
- jaundice (yellowing of skin, gums or eyes) and red, itchy skin

Contraindications: 1) in gastrointestinal bleeding, blood dyscrasia, cardiac, hepatic or renal impairment (insufficiency), dehydration, hypovolaemia or hypotension 2) Concurrent use of potentially nephrotoxic drugs (e.g. aminoglycosides, diuretics) should be avoided with these agents. 3) Not advisable in pregnant animals and animals nearing the oestrus as COX-2 induction is necessary for ovulation and implantation of the embryo. 4) Nearing term, as they delay the parturition (Wallace *et al.*, 2008).

Specific nonsteroidal anti-inflammatory drugs of veterinary importance:

Aspirin is used in veterinary medicine primarily for the relief of mild to moderate pain associated with musculoskeletal inflammation or osteoarthritis. In cats, aspirin may be used for its anti-platelet effects in thromboembolic disease, every 48 hr, to allow for prolonged metabolism. Vomiting and melena may be seen at higher doses. Aspirin overdose in any species can result in salicylate poisoning, characterized by severe acid-base abnormalities, hemorrhage, seizures, coma, and death (Paterson *et al.*, 2008).

Acetaminophen has little ulcerogenic potential, with no effect on platelets or bleeding time. It is more effective in inhibiting COX-3, in the brain rather than in the periphery.

Dose-dependent adverse effects include depression, vomiting, and methemoglobinemia. Use in cats is contraindicated due to a lack of glucuronosyl transferase and the potential for hemolytic anemia and centrilobular hepatic necrosis (Jaeschke *et al.*, 2014).

Meloxicam is recommended to dogs, as a one-time loading dosage of 0.2 mg/kg, PO, followed by 0.1 mg/kg, PO, SID. Once a therapeutic effect is seen, the dosage can be titrated to the lowest possible dose. Once absorbed, meloxicam is highly protein bound

(97%) and has a relatively long elimination half-life (12+ hr). GI safety appears to be greater for meloxicam than for nonspecific NSAID, and meloxicam has been shown to be chondroneutral in rodent studies (Enberg *et al.*, 2006).

Carprofen is approved to manage pain and inflammation associated with osteoarthritis and acute pain associated with soft-tissue and orthopedic surgery in dogs. The exact mechanism of action of carprofen is unclear. Although it has greater selectivity for COX-2 over COX-1, carprofen is considered a weak COX inhibitor. Labrador Retrievers are most susceptible for hepatopathies with carprofen, although a true breed predisposition has not been established (Raekallio *et al.*, 2006).

Flunixin meglumine is used for pain relief in the treatment of colic. It is used for protection from septic/endotoxic shock due to any gastro-intestinal insult either post-surgical or medical such as in cases of peritonitis or diarrhoea. Chronic flunixin meglumine administration in dogs result in severe GI ulceration and renal damage (Luna *et al.*, 2007).

Piroxicam is used for pain due to osteoarthritis., and many types of tumors in dog and cats, including nasal epithelial tumors, mammary tumors, colorectal tumors, oral squamous cell carcinoma, oral melanoma, prostatic carcinoma, transitional cell carcinoma (TCC) of the urinary bladder, osteosarcoma and some rectal neoplasms (Milne and Twomey, 1980).

Phenylbutazone is generally a safe and effective drug in the horse, in which it is commonly used for lameness, resulting from soft tissue injury, muscle soreness, bone and joint problems, and laminitis. Phenylbutazone may be given intravenously or orally; pain relief and temperature reduction usually starting within one to two hours. In dogs it is for the long-term management of chronic pain particularly due to osteoarthritis. It can cross the placenta and is also found in milk. It should be avoided or used with caution in pregnant or nursing animals. It may affect the blood levels and duration of action of phenytoin, penicillin G, sulfonamides, sulfonylurea antidiabetic agents, barbiturates, promethazine, rifampin, chlorpheniramine, diphenhydramine etc. (Doucet *et al.*, 2008).

Nimesulide is used in dogs for relief of pain associated with musculo-skeletal inflammation. It is not indicated for use in puppies younger than 4 months/dogs under 5kg; cats, and pregnant and lactating bitches (Gupta *et al.*, 2000).

Ketoprofen is most commonly prescribed for musculoskeletal pain from soft tissue injury, osteoarthritis or other bone and joint problems. It is a potent inhibitor of COX and bradykinin and may also inhibit some lipoxygenases. Its efficacy is comparable to that of opioids in the management of pain following orthopedic and soft-tissue surgery in dogs. It may be used to reduce or control fevers due to viral or bacterial infections. In dogs and cats, it is used for the short-term management of post-surgical pain and occasionally the longer-term management of chronic pain particularly due to osteoarthritis. It can be also used in the management of colic for protection from bacterial toxins (endotoxemia) (Julou *et al.*, 1976).

Aceclofenac has a faster, more potent analgesic, antipyretic and anti-inflammatory activities. It is superior from other common NSAIDs as it has selectivity for COX-2, and is well tolerated, with better GI tolerability and improved cardiovascular safety when compared to other selective COX-2 inhibitors. It also shows increased matrix component synthesis and protection of chondrocytes against apoptosis. It efficiently interferes with neutrophils adhesion to endothelium and this effect may represent an additional relevant mechanism in its anti-inflammatory activity (Galligan *et al.*, 2016).

Many of the commercially available NSAIDs formulations are also available in combination with other suitable agents for their synergistic action in pain relieving. These include muscle relaxants like chlorzoxazone, carisoprodol, chlomezanone, methocarbamol, tizanidine and anti-inflammatory enzymes like serratiopeptidase.

CINODs: Naproxcinod is the first in a new class of analgesic and anti-inflammatory drugs called COX-inhibiting nitric oxide donators (CINODs), devoid of renal adverse effects due to nitric oxide moiety. It is indicated for the treatment of acute and chronic nociceptive pain, such as post-operative and arthritic pain (Fiorucci and Distrutti, 2011).

Piprants: Grapiprant is the first piprant (a prostaglandin EP4 receptor antagonist) class of anti-inflammatory and analgesic drug. It acts by specifically blocking the EP4 receptor which is the primary mediator of osteoarthritis pain in dogs and is approved as a veterinary drug by FDA for the control of pain and inflammation associated with osteoarthritis (Kirkby *et al.*, 2016).

Adjuvant analgesic drugs: They are generally not considered to be primary first choice analgesics, but used in combination with other analgesic drugs in acute pain states to manage severe pain, so as to reduce the dose of the primary analgesic

Methocarbamol is a muscle relaxant that exerts its effect by acting on the CNS rather than on the muscles themselves; may relieve muscle tension associated with arthritis in pets. It has weak sedative properties and may make the urine appear darker.

Xylazine and Medetomidine hydrochloride – If given by intramuscular injection at less than sedative doses, are effective pain relievers.

NMDA Receptor Antagonists: They block pain by binding to the N-methyl-D-aspartate (NMDA) receptor. These include ketamine, dextromethorphan, memantine, and amantadine. Ketamine, commonly used as a general anesthetic in cats, reduces pain when it is applied to the skin as a specialty compounded gel or paste. Amantadine, originally an antiviral compound is most commonly used to treat drug reactions that affect coordination (extrapyramidal reactions) and pain in dogs. Side effects are may include agitation or diarrhoea (Parsons *et al.*, 1999).

Gabapentin is a structural analogue of GABA, an inhibitory neurotransmitter. It is originally a newer anticonvulsant, used in dogs and cats for the treatment of chronic pain, particularly of neuropathic origin and

also used in chronic arthritic pain and pain associated with malignancy. It appears to be most effective when combined with other types of analgesic agents, as with NSAIDs, permitting the use of lower doses. The most common side effects are mild sedation and ataxia. Care to be taken in animals with decreased liver or renal function. It should not be discontinued abruptly because withdrawal may precipitate seizures or rebound pain. The dosage should be decreased over the course of two to three weeks. It crosses the placenta and gets excreted in milk, thus needs careful monitoring during pregnancy or lactation.

Local anesthetics are peripherally acting analgesics. Long acting agent bupivacaine is used along with lidocaine for long acting pain relief. A single dose of bupivacaine injected at a local site will provide local analgesia for 6-10 hours. Lidocaine is administered as an intravenous constant rate infusion (50-70µg/kg/minute in dogs, 10µg/kg/min in cats) is effective in the treatment of neuropathic pain, periosteal and peritoneal pain. It may also reduce the opioid requirement after surgery when administered as constant rate infusion.

Corticosteroids are the most effective blockers of inflammation and resulting pain. However, they all have major side effects when given over extended periods of time. When they must be used, they should be given in the minimal amount that will control and inflammation and should not be given more than two or three times a week.

Other adjunctive drugs less commonly employed for the relief of chronic pain can include chondroprotectives, anxiolytics and sedatives like benzodiazepines (eg: diazepam, midozolam), tricyclic antidepressants (e.g. amitryptilline, imipramine), doxycycline, omega-3 fatty acids, magnesium, immunonutritional modifiers and bioflavinoids.

Table. Drugs with analgesic potential in clinical use and the dosages:

Drug	Dosage
Analgesic	
Acetaminophen	**Cattle:** 50 mg/kg PO, followed by 30 mg/kg PO q6h; **Dog:**15 mg/kg q8h PO-
Amantadine	**Dog:** 3-5 mg/kg q12h, PO; **Cat:**3 mg/kg q24h PO, up to 5 mg/kg in some cases
Gabapentin	**Horse:** Neuropathic pain: 2.5 mg/kg q12h PO; **Dog:** Neuropathic pain: Start with 5-15 mg/kg q12h PO, up to 40 mg/kg q8-12h PO; **Cat:** Neuropathic pain: 5-10 mg/kg q12h PO.
Pregabalin	**Horse:** 4 mg/kg PO q8h; **Dog:** Neuropathic pain: 4 mg/kg q12h PO; **Cat:** Neuropathic pain: Start with 2 mg/kg q12h PO, up to 4 mg/kg q12h PO

Analgesic Opioid	
Tramadol	**Horse:** 2mg/kg IV (slowly) and 4-5 mg/kg PO; **Dog:** 5 mg/kg q6h-8h PO. Injectable form 4 mg/kg IV q6-8h; **Cat:** Start at 2 mg/kg and up to 4 mg/kg q8-12h PO. Injectable form 2mg/kg IV and 2-4 mg/kg SC q8h.
Hydrocodone bitartrate	**Dog:** 0.5 mg/kg q8-12 hr PO.
Hydromorphone	**Dog:** 0.22mg/kg IM or SC. Repeat every 4-6 hours or as needed for pain treatment. 0.1-0.2 mg/kg IV, repeated every 2 hours or as necessary. A dose of 0.1 mg/kg may be used with acepromazine as a preoperative sedative. **Cat:** 0.1-0.2 mg/kg SC or IM, or 0.05-0.1 mg/kg IV q2-6h (as needed).
Acetaminophen + codeine	**Dog:** 0.5-1.0 mg/kg q4-6h PO.
Buprenorphine hydrochloride	**Horse:** 0.005-0.01 mg/kg; **Dog:** 0.006-0.02 mg/kg q4-8h IV, IM, or SC. For analgesia 0.03-0.04 mg/kg SC; **Cat:** 0.01-0.02 mg/kg IV or 0.02 mg/kg IM. Duration 4-6 hours.
Butorphanol tartrate	**Cattle:** 0.01-0.02 mg/kg IV in combination with xylazine; **Horse:** 0.2-0.4 mg/kg q3-4h IV. Some instances, lower dose of 0.02-0.1 mg/kg IV or 0.04-0.2 mg/kg IM have been used; **Dog:** 0.2-0.4 mg/kg q2-4h IV, IM or SC or 1-4 mg/kg q6h PO; **Cat:** 0.2-0.8 mg/kg q2-6h IV or SC or 1.5 mg/kg q4-8h PO.
Fentanyl citrate	**Small ruminants:** 5-10 mcg/kg IV; **Dog:** 0.005-0.01 mg/kg q2h IV, IM or SC
Meperidine	**Dog:** 5-10 mg/kg IV or IM, every 2-3 hours; **Cat:** 3-5 mg/kg IV or IM every 2-4 h.
Methadone hydrochloride	**Horse:** 0.15 mg/kg IV, or oral q6-8h; **Dog:** 0.1-0.5 mg/kg IV, or 0.5-2.2 mg/kg q3-4h SQ or IM; **Cat:** 0.3-0.6 mg/kg q3-4h IV, SQ or IM
Morphine sulfate	**Cattle:** Use is controversial still 0.05-0.1 mg/kg IV and up to 0.4 mg/kg IV have been used to treat pain; **Horse:** Pain 0.5-1 mg/kg IV or IM; **Dog:** 0.5 mg/kg q2h IV or IM; **Cat:** 0.1-0.2 mg/kg IM, IV or SC q3-6h (Cats are very sensitive).
Oxymorphone hydrochloride	**Dog:** 0.1-0.2 mg/kg IV, SC or IM. Re dose with 0.05-0.1 mg/kg q1-2h; **Cat:** 0.1-0.2mg/kg IV, SC or IM. Re dose with 0.05-0.1 mg/kg q1-2h.

Pentazocine	**Dog:** 1.65-3.3 mg/kg q4h IM or as needed; **Cat:** 2.2-3.3 mg/kg q4h IM, IV or SC.
Remifentanil	**Dog:** 0.20 mcg/kg/min up to 1 mcg/kg/min; **Cat:** 2.5 mcg/kg bolus inj. followed by 0.2-0.24 mcg/kg/min.
Sufentanil citrate	**Dog:** 2 mcg/kg IV up to 5 mcg/kg; **Cat:** 2 mcg/kg IV up to 5 mcg/kg
Analgesic NSAIDs	
Aspirin	**Cattle:** 100 mg/kg q12h PO; **Horse:** 25-50 mg/kg q12h PO (up to 100 mg/kg PO per day; **Dog:** Analgesia: 10 mg/kg q12h PO; **Cat:** 10 mg/kg q48h PO.
Carprofen	**Cattle:** 1.4 mg/kg SC, IV; **Horse:** 0.7 mg/kg q24h IV; **Dog:** 2.2 mg/kg q12h PO or 4.4 mg/kg q24h PO; **Cat:** 4 mg/kg given once by injection or 0.5 mg/kg q24h PO for long term use.
Deracoxib	**Dog:** 3-4 mg/kg once daily for 7 days. Chronic use: 1-2 mg/kg once daily PO; **Cat:** 1 mg/kg single dose PO.
Etodolac	**Horse:** 23 mg/kg q24h PO; **Dog:** 10-15 mg/kg once daily PO or 10-15 mg/kg SC.
Firocoxib	**Calves:** 0.5 mg/kg PO or IV q24h; **Horse:** 0.1 mg/kg q24h Po for up to 14 days; **Dog:** 5 mg/kg once daily PO.
Flunixin meglumine	**Cattle:** 1.1-2.2 mg/kg (slowly) once a day for up to 3 days IV. Combination with florfenicol 40mg/kg florfenicol and 2.2 mg/kg flunixin SC; **Horse:** 1.1 mg/kg q24h up to 5 days IV or IM. Paste: 1.1 mg/kg q24h PO; **Dog:** 1.1 mg/kg once IV, IM or SC; 1.1 mg/kg/day 3 day/week PO; **Cat:** 1.1 mg/kg once IV, IM or SC; 1.1 mg/kg/day 3 day/week PO.
Ibuprofen	**Cattle:** 14-25 mg/kg/day PO; **Horse:** 25 mg/kg q8h PO up to 6 days.
Ketoprofen	**Cattle:** 3 mg/kg/day IV or IM for up to 3 days; **Horse:** 2.2-3.3 mg/kg/day IV or IM; **Dog:** 1 mg/kg q24h PO for up to 5 days; **Cat:** 1 mg/kg q24h PO for up to 5 days.
Ketorolac tromethamine	0.5 mg/kg q8-12h PO, IM or IV
Meclofenamic acid	**Horse:** 2.2 mg/kg q24h PO; **Dog:** 1.1 mg/kg/day up to 5 days PO.

Meloxicam	**Cattle:** 0.5 mg/kg q24h IV, IM or SQ; **Horse:** 0.6 mg/kg q24h IV or PO; **Dog:** 0.2 mg/kg initial loading dose PO, SC or IV and then 0.1 mg/kg q24h thereafter; **Cat:** 0.05 mg/kg q24h PO with reduction in dose if treatment is pursued.
Naproxen	**Horse:** 10 mg/kg q12h PO; **Dog:** 5 mg/kg initially, then 2 mg/kg q48h PO.
Phenylbutazone	**Cattle:** 17-25 mg/kg loading dose, then 2.5-5 mg/kg q24h or 10-14 mg/kg q48h PO or IV; **Horse:** 4.4-8.8 mg/kg/day (generally 2g to 4g per horse) PO; Injection: 2.2-4.4 mg/kg/day for 48-96 hours IV; **Dog:** 15-22 mg/kg q8-12h (44 mg/kg/day; 800 mg/dog maximum) PO or IV; **Cat:** 6-8 mg/kg q12h IV or PO.
Piroxicam	**Dog:** 0.3 mg/kg q48h PO; **Cat:** 0.3 mg/kg q24h PO.
Robenacoxib	**Dog:** 1-2 mg/kg q24h PO; **Cat:** 1-2.4 mg/kg PO once per day.
Tepoxalin	**Dog:** 10 mg/kg q24h PO; **Cat:** 10 mg/kg.
Nimesulide	**Dog:** 5 mg/kg PO once daily for 3-5 days.
Tolfenamic acid	**Cattle:** 2 mg/kg IM once daily; **Dog:** 4 mg/kg PO once daily for 3 days; 4 mg/kg SC or IM may be repeated after 24 hours; **Cat:** 4 mg/kg PO once daily for 3 days; 4 mg/kg SC or IM may be repeated after 24 hours.
Anti-inflammatory corticosteroids	
Dexamethasone	**Cattle:** 0.04-0.15 mg/kg per day IV or IM; Total dose 5-20 mg/animal; **Horse:** 0.05-0.1 mg/kg IV or IM q24 h; **Dog:** 0.07-0.15 mg/kg q12-24h IV, IM or PO; **Cat:** 0.15 mg/kg q12-24h IV, IM or PO.
Flumethasone	**Cattle:** 1.25-5 mg/animal single dose IV or IM; **Horse:** 1.25-2.5 mg per animal as a single dose IM or IV; **Dog:** 0.15-0.3 mg/kg q12-24h PO, IV, IM or SC; **Cat:** 0.15-0.3 mg/kg q12-24h PO, IV, IM or SC.
Hydrocortisone	**Horse:** 5 mg/kg q12h IV; **Dog:** 2.5-5 mg/kg q12h PO; **Cat:** 2.5-5 mg/kg q12h PO.
Isoflupredone acetate	**Cattle:** 10-20 mg total dose per animal q12-24h IM; **Horse:** 5-20 mg total dose per animal q12-24h IM.
Methylprednisolone	**Dog:** 0.22-0.44 mg/kg q12-24h PO. Methylprednisolone acetate: 1 mg/kg (or 20-40 mg/dog) IM q1-3wk; **Cat:** Methylprednisolone: 0.22-0.44 mg/kg q12-24h PO.

Prednisone	**Cattle:** 100-200 mg total dosage IM; **Horse:** 100-400 mg per horse (0.22-0.88 mg/kg) as a single dose IM to be repeated every 3-4 days; **Dog:** 0.5-1 mg/kg q12-24h IV, IM or PO then taper to q48h at a dose of 0.3-0.5 mg/kg.
Prednisolone acetate	**Horse:** 100-200 mg total dosage IM; **Dog:** 0.5-1 mg/kg q12-24h IV, IM or PO then taper to q48h at a dose of 0.3-0.5 mg/kg; **Cat:** 0.5-1 mg/kg q12-24h IV, IM or PO then taper to q48h at a dose of 0.3-0.5 mg/kg.

(Source: Papich (2016) Saunders handbook of veterinary drugs: small and large animal, 4th edn. Elsevier, Missouri, USA.)

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