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Osteoarthritis in brief (Part2) - Management

Summary

Osteoarthritis is a debilitating condition affecting up to 20% of canine and 60% feline patients. Whilst diagnosis is fairly straightforward, the aetiology behind the disease process and therefore the treatment strategies are not. Multimodal management is the mainstay of controlling clinical signs and ensuring patient comfort, however this involves potentially long-term pharmacologic and dietary control and requires significant client compliance.

Research into disease pathogenesis and treatment strategies is ongoing but evidence, especially relating to many therapies and nutritional supplements is currently lacking. Genetic research continues as does that into mesenchymal stem cell therapy and cartilage repair and regeneration but clinical "cure" remains a distant objective.

This second article aims to discuss multimodal management of the condition in more detail, including physical therapy, dietary management, analgesia and surgical strategies. It will briefly introduce the concept of cellular and targeted pharmacologic treatment and will hopefully encourage readers to undertake further reading on these topics.

Introduction

Whilst the first article (Companion Animal, XXXX 2016) covered the aetiology, pathophysiology, and diagnosis of osteoarthritis (OA), this article aims to discuss the management and therapeutic options available for treatment of the osteoarthritic patient. The goals of OA therapy are to manage pain, maintain function and joint range of motion, and maintain or restore normal activity (Davidson & Kerwin, 2014). In general terms management may be surgical or non-surgical with the latter involving a combination of strategies to provide relief including analgesia, weight management, exercise control, physical therapy and the use of nutraceuticals. Cellular therapies are also now being developed and will be mentioned briefly.

Weight management

Obesity and increased body weight are risk factors for developing OA (Figure 1). In some studies there is evidence to suggest that reducing obesity in dogs with clinical signs of OA such as lameness may lead to a clinical improvement (Impellizeri et al, 2000; Budsberg & Bartges, 2006) and in human studies many symptoms are relieved through weight reduction/obesity management alone (Messier, 2008). The incidence of obesity in client-owned pets is increasing (German, 2006) and achieving weight loss is challenging, requiring both patience and sensitive client-education to encourage the feeding of calorie-restricted diets (German et al., 2007). In one study in dogs, the loss of between 6-8% of body weight has been shown to significantly improve limb function using objective (force-plate) measures (Marshall et al., 2010) and in a non-blinded prospective study of 9 overweight dogs with hip OA, an 11-18% reduction in bodyweight correlated with a decreased severity of hind limb lameness (Impellizeri, 2000). Mlacnik et al (2006) demonstrated improved mobility and weight loss in a prospective randomized clinical trial of 29 overweight dogs involving caloric restriction and physiotherapy. Kealy and colleagues reported that a long-term

25% restriction in food intake of dogs delayed the onset of chronic disease, including OA, and increased lifespan, while the prevalence and severity of OA was also reduced (Kealy et al, 2000, Kealy et al, 2002). In a lifetime study on a cohort of Labrador retrievers housed in pairs with one fed ad-libitum (control) and one fed at 25% diet restriction (diet-fed) and with similar distribution of hip-laxity scores as ascertained by Penn-HIP, those diet-fed had a 4% incidence of radiographic hip osteoarthritis at 2 years old, compared to 42% of the control dogs. By 5 years old, 13% of diet-fed dogs had evidence of hip OA compared with 52% of control fed. The diet-fed Labradors lived longer and at end-of-life 50% had radiographic evidence of hip osteoarthritis compared to 83% of control dogs (Smith et al, 2012).

Physical therapy and exercise management

Physical methods of rehabilitation for the OA patient include heat, cold, water, sound, electricity, massage and exercise therapy. Overall, benefits relate to an increased blood flow to the affected areas, reduction or resolution of inflammation, preventing or minimizing muscle atrophy, preventing periarticular contraction and the provision of positive psychologic effects for both patient and owner (Johnston et al, 2008). The following gives a brief overview of these methods but the reader is referred to other sources for in-depth discussions of physical therapy (Johnston et al, 2008; Millis & Levine, 2014; Saunders et al, 2005).

Pain and stiffness associated with joint pain and osteoarthritis may lead to lameness or reduced activity, culminating in a loss of muscle mass and limb strength (Davidson & Kerwin, 2014). Active exercise improves muscle strength, endurance, cardiovascular function and co-ordination and also reduces joint stiffness, muscle atrophy and bodyweight (Clark & McLaughlin, 2001; Taylor et al, 2004; Pamoski & Brandt, 1984). Cartilage loading during weight bearing may also improve cartilage metabolism and proteoglycan synthesis (Millis & Levine, 1997; Pamoski & Brandt, 1984). In geriatric patients with OA, controlled, low-impact exercise has been shown to improve pain and function scores (Hudson & Hulse, 2004). A regular exercise program of low-impact activity including controlled lead walking and walking through water can help maintain muscle strength whilst minimising joint stress. Boisterous impact-activities and bursts of uncontrolled activity should be avoided. In patients with pelvic limb disease sit-to-stand exercises, gentle uphill walking or controlled stair climbing may be used to improve pelvic limb musculature (Davidson & Kerwin, 2014). Several shorter periods of exercise are usually preferred over a single long one (Johnston et al, 2008). Hydrotherapy reduces the amount of weight the patient must support during activity, with water depths above the level of the greater trochanter reducing the weight borne by approximately 50% (Johnston et al, 2008). Use of an underwater treadmill improves cardiovascular endurance and muscle strength whilst reducing pain, improving balance and improving joint range of motion (ROM) (Levine et al, 2014)

Passive stretching and passive ROM exercises may be utilised to improve joint function in patients with OA (Figure 2). When evaluating the level of passive ROM exercises to advise for a patient it is important to be aware that in painful

joints ROM is reduced and, if the pain can be controlled, ROM is likely to improve. In cases where joint stiffness is evident, pain is often encountered towards the end of normal ROM. If both joint stiffness and pain are present it is useful to assess which factor is dominant and to aim to prioritise treatment of that (Saunders et al, 2005). ROM exercises should always be performed within a patient's comfort zone; excessive manipulation may lead to reflex inhibition, reduced limb use, tissue fibrosis and a delay in return to normal function (Johnston et al, 2008). Passive ROM exercises may be combined with the use of massage and heat therapy to provide increased levels of comfort during the rehabilitation periods, and analgesics are often used to improve patient comfort (Tanger 1984). Stretch and balance exercises that focus on weight shifting help with overall balance and proprioception (Davidson & Kerwin, 2014).

Local hypothermia can be useful to treat patients with acute inflammation. Application of cold packs promotes vasoconstriction and skeletal muscle contraction and reduces nerve conduction, in turn reducing oedema, improving venous return and promoting mild analgesia. Following the resolution of acute inflammation and in more chronic cases of OA, moist heat may be used, again often benefitting the patient prior to passive and active exercise therapy. An increase in local blood flow through local vasodilatation and increased absorption of extravasated fluids helps improve local nutrient delivery to the tissues and the heat will also increase compliance of joint capsule, tendons, and scar tissue reducing joint stiffness and contributing to pain relief (Johnston et al, 2008).

Laser therapy, therapeutic ultrasound, transcutaneous electrical nerve stimulation and extracorporeal shockwave therapy have been evaluated as ancillary treatments although the current clinical evidence for their use in veterinary medicine is limited. Readers are referred to more specialised texts such as Millis & Levine (2014) for further information.

Pain management

The majority of treatment of OA is directed towards palliating the joint pain associated with the disease. It must be remembered that signs of OA are not consistent and there is no single solution that can be recommended in all cases. Lameness, pain and clinical signs may be severe in the light of minimal radiographic change and vice versa. The severity of the signs will also depend on the amount of stress (use) the tissues both within and around the joint are exposed to. Acute and chronic pain may be present simultaneously, necessitating a multimodal pharmacologic and non-pharmacologic approach (Johnston et al, 2008).

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) with their analgesic, anti-inflammatory and anti-pyretic effects are the most frequently prescribed medication to treat OA. NSAIDs have been shown to be clinically effective to treat OA pain in a number of studies (Innes et al, 2010; Mansa, 2007; Sanderson et al, 2009; Payne-Johnson et al, 2015) and a systematic review published in 2007 found a high level of comfort for the use of meloxicam as clinically efficacious for

treatment of OA in dogs (Aragon et al, 2007). In general, although there is not major evidence that any one NSAID is clinically superior to another it is likely that in specific individuals, one NSAID may work better than another (Johnston, 2008). In a clinical setting, it may be prudent to alter the NSAID prescribed if one does not seem to be achieving the desired outcome, rather than changing the entire analgesic plan (KuKanich, 2012).

When switching from one NSAID to another a washout period is recommended in order to avoid the possibility of adverse effects. These periods are arbitrarily based on the half-life of the drug, and presume that the majority of a drug dose will have been eliminated within 4-5 half lives. For most NSAIDs, plasma half-lives are between 1-24 hours, although in the case of mavacoxib is much longer, extending to 39 days. Conservative washout periods for NSAIDs (with the exception of aspirin and mavacoxib) are 5-7 days (Lascelles et al, 2005; Ryan et al, 2007).

NSAIDs work through inhibition of the cyclo-oxygenase (COX) pathway; the key enzyme in the formation of prostaglandins from arachidonic acid. Prostaglandin E₂ (PGE₂) has a number of roles in enhancing the development of OA including lowering the nociceptive threshold, promotion of synovitis, enhanced formation of matrix metalloproteinases (MMPs) that stimulate cartilage degradation and reduce chondrocyte activity, thereby preventing extracellular matrix synthesis and repair. In addition to this, COX inhibition within the central nervous system reduces the arachidonic acid catalysed wind-up of NMDA receptors, reducing central sensitisation and chronic pain (see previous article).

NSAIDs available for use in the UK and their recommended dose rates are listed in Table 1.

Other analgesics

Due to the complex pain mechanisms present in OA, a combination of drug therapies may be recommended in cases where NSAIDs combined with physical therapy do not adequately control clinical signs. Whilst there are a number of drugs that may be combined with NSAIDs, clinical efficacy of them all has not necessarily been proven and there are only a few studies that support their veterinary clinical use. If used, these drugs are prescribed off-licence and owner consent must be sought.

Amantadine is an N-methyl-D-aspartate (NMDA) receptor antagonist and acts to control central sensitisation and neuropathic/chronic inflammatory pain. In a single study, Lascelles et al (2008) reported the use of amantadine in a multimodal analgesic regimen to alleviate refractory OA pain in dogs. 31 dogs with ongoing pelvic limb lameness despite NSAID therapy were included in a blinded, randomized, placebo controlled trial. Over the 42-day study period dogs receiving amantadine were significantly more active and the conclusion was that amantadine may be a useful clinical adjunct therapy for the clinical management of canine OA pain. There are two small reports of some clinical benefit in both dogs (Madden, 2014) and cats (Siao, 2011).

Dose rate: dogs 3-5 mg/kg, p.o., q. 24 hours; cats 1-4 mg/kg

Amitriptyline is a tricyclic antidepressant used to treat chronic and neuropathic pain in humans. The drug inhibits neuronal reuptake of serotonin and noradrenaline, increasing the activity of descending inhibitory pathways that modulate afferent nociceptive input (Johnston, 2008). There are no published clinical trials on the clinical use of the drug in veterinary medicine although pharmacokinetic data has been obtained in greyhound dogs (Norkus, 2015).

Codeine is a pro-drug that is metabolized into morphine and codeine-6-glucuronide. It is a schedule II drug (schedule III in combination with paracetamol). Although there are no published data regarding the efficacy of its use in clinical OA it is often used in conjunction with NSAIDs for multimodal analgesia and has been used as rescue analgesia in a clinical trial of canine OA with no adverse effects (Innes et al, 2003).

Doses of 0.5-2 mg/kg, p.o., q. 12 hours in both dogs and cats.

Corticosteroids given either orally or intra-articularly are a controversial treatment for OA and they should never be used in combination with NSAIDs. Intra-articular therapy may provide temporary remission of clinical signs, and is most commonly used in patients with severe end-stage OA signs that are refractory to other treatments (Henrotin et al, 2005) but in some cases chondromalacia may develop and lead to a worsening of the disease process (Murphy et al, 2000). Use should be restricted to approximately 3-4 doses intra-articularly per year to avoid the possible development of these cartilage-damaging effects (Innes, 2012). If septic arthropathy is present corticosteroid treatment is contraindicated.

The use of intra-articular hyaluronan in combination with methylprednisolone has recently been compared with intra-articular autologous conditioned plasma to treat elbow arthritis in dogs (Franklin & Cook, 2013). Each treated group significantly improved with regard to lameness, pain and activity scores on client-based assessment although neither treatment proved to be superior.

Gabapentin is a gamma-aminobutyric acid (GABA) analogue. Although the exact mechanism of action is unknown the effects of gabapentin seem to occur through blockade of voltage-activated calcium channels and interactions with NMDA receptors that are responsible for wind-up in the central nervous system (Sills, 2006). Gabapentin is widely used in human patients to relieve neuropathic pain although, again, peer-reviewed evidence of efficacy in dogs does not exist. A recent case series of three cats with musculoskeletal disease and head trauma reports a potential benefit of long-term treatment with gabapentin in controlling chronic pain (Lorenz et al, 2013).

Dose of 10mg/kg, p.o., q. 8 hours in dogs, and 5 mg/kg in cats.

Paracetamol is a centrally acting analgesic medication with widespread use in human patients with osteoarthritis. The mechanism of action is not known but some interaction with serotonin receptors and opiate pathways may be involved. Paracetamol cannot be used in cats because they lack the glucuronyl transferase enzyme required for drug metabolism. In dogs a dose of 10-15 mg/kg, q. 8-12

hours is recommended, however the only licensed form of this drug in the UK is in combination with codeine as Pardale-V® and this is only licensed for 5 consecutive days. The codeine in this preparation does not survive first pass metabolism so does not appear to add to the analgesic effects of the drug.

Tramadol is an opioid-like analgesic that is metabolised to a number of different active compounds, some acting at opioid receptor sites with others modulating noradrenaline and serotonin receptor uptake. A combination of tramadol with NSAID or paracetamol has been reported to be effective at treating OA pain in people (Johnston et al, 2008) and in one clinical trial, tramadol proved more effective than placebo in treating chronic pain associated with OA (Malek et al, 2012).

Doses of 2-5 mg/kg, p.o., q. 8 hours.

Nutritional supplementation and additional therapeutic agents

Nutraceuticals or dietary supplements are widely advertised as providing clinical benefit to canine and feline patients with OA, however evidence is limited. Due to the potential adverse side effects of non-steroidal anti-inflammatories, and the cartilage degradation effects of intra-articular steroid treatment, ideal management of OA should focus on prevention of the disease and administration of safe long-term solutions to the problem. It has been suggested this prevention and long-term safe strategy may be available in the form of nutrition or dietary supplements (Comblain et al, 2016).

Chondroitin Sulphate and Glucosamine

McCarthy et al (2007) demonstrated that supplementation with chondroitin sulphate and glucosamine improved pain scores in dogs compared to carprofen, although the onset of effect was delayed in comparison. Two other canine studies demonstrated significant improvements in pain compared to placebo in dogs with OA treated with these supplements (D'Altilio, 2007; Gupta, 2012). In contrast, Moreau et al (2003) identified no such benefit of the nutraceutical with subjective and objective measures of improvement only occurring in NSAID-treated dogs.

Polyunsaturated fatty acids

Several *in vivo* studies have evaluated the efficacy of omega-3 fatty acids in dogs with documented OA, with subjective improvements in lameness, ability to rise from rest, and ability to walk, as well as increases in peak force seen in the cases given dietary supplements (Roush, 2010; Fritsch et al, 2010). In other studies, fish-oil supplementation improved peak vertical force and owner quality of life assessments but had no documented effect on pain relief at the end of the study compared to placebo (Hielm-Bjorkman et al, 2012). Administration of fish oil has been shown to reduce inflammatory markers such as arachidonic acid, IL-1, IL-6 and PGE2, which may give reason for their clinical effects (LeBlanc et al, 2008).

Undenatured type II collagen, avocado-soyabean unsaponifiables and green-lipped muscle have all been evaluated with some studies showing positive effects on OA although more evidence for their use is required (Comblain et al, 2016, Rialland et al, 2013, Vendeweerd et al, 2012).

A systematic review of the efficacy of nutraceuticals to alleviate clinical signs of OA in horses, dogs and cats found few rigorous randomised, controlled clinical trials, concluding that evidence for their efficacy was poor except for diets supplemented in omega-3 fatty acids in dogs (Vandeweerd et al, 2012). Comblain et al's (2016) more recent review concluded that whilst NSAIDs remain the mainstay of pharmacologic therapy in cases of OA, dietary supplements may offer additional disease-modification, including anti-inflammatory and chondroprotective effects, without the recognised side effects of long-term pharmacological treatment. Whilst they conclude that nutraceuticals have the potential to provide alternative means of preventing and managing OA in dogs, they do highlight poor oral bioavailability of many supplements and specify that formulations must be altered in order to improve this.

Aragon et al (2007) reviewed clinical trials of treatments for OA in dogs comparing pharmacologic and nutraceutical agents and identified high evidence for the use of meloxicam as a clinically efficacious treatment of OA in dogs. Moderate levels of evidence were available for the use of carprofen, etodolac, pentosan polysulphate, green lipped muscle P54FP, polysulphated glycosaminoglycans and a combination of chondroitin sulphate, glucosamine hydrochloride and manganese ascorbate. Very poor evidence existed for the use of hyaluronan although human studies do suggest reduction in clinical signs and improvements in mobility (Kuroki et al, 2002).

Autologous platelet therapy

The intra-articular injection of autologous platelets is a potentially promising new therapy for OA in dogs. Platelets contain growth factors that have been shown to enhance regenerative processes in osteoarthritic joints. Intra-articular autologous platelet therapy has been documented to provide subjective improvements in human patients with OA and significant improvements in lameness, pain scores and peak vertical force in a randomised, controlled clinical trial in dogs with single joints affected by OA have also been documented (Fahie et al, 2013).

Mesenchymal stem cells

Stem cells are gaining increasing popularity for use in regenerative techniques. Stem cells are undifferentiated cells with the ability to divide indefinitely without losing their properties and will eventually develop to produce specialised cell lines. In equine medicine there are a number of reports advocating the use of stem cells for ligament and tendon injuries with no adverse systemic effects and minimal local tissue reaction. A couple of canine studies have identified improved orthopaedic examination scores in dogs being treated with intra-articular mesenchymal stem cells for OA (Black et al, 2007).

Grapiprant

A more-targeted approach than the use of NSAIDs for treating OA would involve blockage of only the part of the prostaglandin pathway involved in pain and inflammation without altering the protective mechanisms of that pathway.

Prostaglandin E₂ is the most abundant prostaglandin in synovia and is pivotal in the development of joint inflammation and pain (Clark et al, 2008). Grapiprant is a new analgesic and anti-inflammatory drug that is a highly potent and selective antagonist of the PGE₂ EP4 receptor in rodents, humans and dogs. (Nakao et al, 2007). FDA approval has been granted for the drug for use in the treatment of the pain and inflammation linked to OA and it will be available in the US in Autumn 2016.

Anti-Nerve Growth Factor Antibody

Nerve growth factor (NGF) is required in the adolescent nervous system for development and maintenance of sensory and sympathetic neurons. In adults, the growth factor has been identified as pro-nociceptive with modulatory effects on the tyrosine-kinase receptor and is involved in the sensation of pain including that of OA (Lascelles et al, 2015). In canine studies, anti-NGF antibodies have been demonstrated to alleviate pain in dogs with OA for up to four weeks (Lascelles et al, 2015). Whilst numbers in these trials are low (35 dogs in total) and adequate information regarding side effects and long-term effects are lacking, this may be a further useful adjunct to the management of OA in the canine patient.

Further detailed information on cellular therapies and targeted pharmacologic approaches to canine joint treatment can be found in Perry (2016a & b).

Surgical Management

The goals of surgical treatment of OA are pain relief, amelioration or removal of pathologic changes associated with OA and maintenance of maximal joint function (Cook & Payne, 1997). Whilst salvage surgeries to treat OA may be performed, prevention is better than cure, and correction of those conditions known to cause OA is important to reduce or slow the development of the disease (Box 1).

Reported surgical options for treatment include synovectomy, cartilage grafting and osteotomies, whilst salvage procedures include excision arthroplasty, arthrodesis and joint replacement (Cook & Payne, 1997). The procedure chosen will depend on the joint affected and the disease process present; end-stage joint disease may require a salvage procedure, whilst osteochondral flap excision and debridement of the underlying subchondral bone bed from the humeral head will manage discomfort and reduce OA development in the shoulder joint (Martinez, 1997).

Arthroscopic evaluation and treatment is a minimally invasive method of quantifying OA change and identifying the severity of cartilage damage (article 1). Debridement of damaged cartilage, joint lavage, synovectomy and releasing procedures are all performed arthroscopically in human medicine to treat the OA-affected joint (Cook & Payne, 1997) and cartilage resurfacing using grafts has been undertaken in veterinary patients to treat osteochondral lesions (Cook et al, 2008; Fitzpatrick et al, 2010 & 2012a). Sliding humeral osteotomy and unicompartamental cartilage resurfacing are options available to treat medial compartmental disease of the elbow joint, where previously total elbow

replacement may have been necessary (Fitzpatrick et al, 2015; Franklin et al, 2014).

Surgical salvage includes treatments such as excisional arthroplasty, total joint replacement and amputation. Whilst total hip replacement is commonplace in small animal practice, elbow replacements are less so, most likely due to the high complication rates associated with replacement of the complex elbow joint. Excision arthroplasty is a feasible option for the coxofemoral joint and digits, whilst it is a poor option for functional outcome in the shoulder. Arthrodesis is an option to provide good functional outcome in low-motion joints such as the carpus and tarsus. In higher motion joints results may be less satisfactory although stifle arthrodesis and shoulder arthrodesis have been reported with reasonably acceptable outcomes (Cofone et al, 1992; Fitzpatrick et al 2012b).

Conclusion

OA is a condition that affects large numbers of dogs and cats. Whilst current strategies often focus on the management and treatment of OA, our focus for the future should be on disease prevention and disease modification. Appropriate and early management of primary orthopaedic disease, client education and continuing research into disease-modifying agents are a priority, as is further research and development into ways to address the condition in order to improve quality of life and avoid the necessity for salvage procedures.

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Congenital conditions	Acquired conditions
Osteochondritis dissecans (OCD)	Cranial cruciate ligament disease
Canine developmental elbow disease Fragmented medial coronoid process Elbow OCD Ununited anconeal process	Joint Trauma Articular fractures Joint luxation Ligamentous injury
Canine hip dysplasia	
Canine patella luxation	

Box 1: Congenital and acquired conditions leading to the development of osteoarthritis (adapted from Martinez, 1997 and Martinez & Coronado, 1997)

Table 1: NSAIDs licensed for use in the UK. The dosage is that for patients with pain and inflammation associated with osteoarthritis (Data from the VMD website, August 2016 and BSAVA Formulary, 8th ed)

Drug	Dosage (UK licensed)	Indications	Mechanism of action
Carprofen	Oral and injectable 4 mg/kg once daily or 2 mg/kg twice daily for 7 days reducing to 2 mg/kg once daily subject to clinical response	Control of postoperative pain and inflammation following surgery and reduction of chronic inflammation, e.g. degenerative joint disease, osteoarthritis. In cats carprofen is only licensed as a single perioperative dose for the control of postoperative pain.	Inhibition of COX enzyme; in vitro selective against COX-2
Cimicoxib	2 mg/kg orally once daily	For the relief of pain and inflammation associated with OA in dogs and the control of peri-operative pain in soft tissue and orthopaedic surgeries in dogs	A coxib class drug that selectively inhibits COX-2, with a significant sparing effect on COX-1 enzyme synthesis
Firocoxib	5 mg/kg orally once daily	For the relief of pain and inflammation associated with OA in dogs and the control of postoperative pain in soft tissue and orthopaedic surgeries in dogs	Inhibition of COX activity; in vitro studies show high selectivity for COX-2 in canine blood
Ketoprofen	Dogs - 2 mg/kg s.c., i.m., i.v. once daily, may be repeated for up to 3 consecutive days; 0.25 mg/kg orally once daily for up to 30 days in total; 1 mg/kg orally once daily for up to 5 days. Cats - 2 mg/kg s.c. once daily, may be repeated for up to 3 consecutive days; 1 mg/kg orally, once daily for up to 5 days. Oral dosing for 4 days may follow a single injection of ketoprofen on day 1	Relief of acute pain from musculoskeletal disorders and other painful disorders in the dog and cat. Management of chronic pain from osteoarthritis in the dog. Ketoprofen is not COX-2 selective and is not authorized for preoperative administration to cats and dogs.	COX-1 and LOX inhibition
Mavacoxib	2 mg/kg orally. Give the first two doses 14 days apart then monthly (not to exceed 6.5 months of therapy)	For the treatment of pain and inflammation associated with degenerative joint disease in dogs at least 12 months old in cases where continuous treatment exceeding one month is indicated	Preferential inhibition of COX-2 mediated PG synthesis
Meloxicam	Dogs - 0.2 mg/kg injectable or oral once, followed by 0.1 mg/kg oral suspension once daily Cats - 0.2 mg/kg injectable or oral once, followed by 0.05 mg/kg oral suspension once daily	Control of acute and chronic pain of musculoskeletal disorders and inflammation associated with OA in dogs. Reduction of postoperative pain and inflammation following orthopaedic or soft tissue surgery	Preferential inhibition of COX-2
Paracetamol + codeine	1 tablet per 12 kg bodyweight three times daily (treat for a maximum of 5 days)	Control of mild to moderate pain	Mechanism of action unknown
Phenylbutazone	2-20 mg/kg orally q. 8-12 hours	Management of mild to moderate pain and	COX-1 inhibitor

		inflammation in osteoarthritic conditions. Not for peri-operative use.	
Robenacoxib	2 mg/kg s.c. once daily for a maximum of 2 doses; 1-2 mg/kg orally, once daily (in cats for up to 6 days).	Alleviation of inflammation and pain in both acute and chronic musculoskeletal disorders, and the reduction of postoperative pain and inflammation following orthopaedic and soft tissue surgery in dogs. Treatment of acute pain and inflammation in cats.	COX-2 selective
Tolfenamic acid	Dogs - 4 mg/kg i.m., s.c., may be repeated once after 24h; 4 mg/kg orally for 3 days. Oral dosing can be repeated every 7 days in dogs Cats - 4 mg/kg s.c., may be repeated once after 24h; 4 mg/kg orally. for 3 days.	Alleviation of inflammation and pain in dogs and cats. Also used in the management of chronic locomotor disease in dogs	COX inhibition, direct action of antagonism on PG receptors

COX - cyclo-oxygenase; LOX - lipoxygenase; OA - osteoarthritis; PG - prostaglandin

Figure 1 – Obesity is a major factor in osteoarthritis and weight loss remains one of the best treatment strategies for these dogs

Figure 2 (a and b) – Passive range of motion exercises such as joint flexion and extension can easily be performed at home

Figure 3 (a and b) - Lateral radiographs of the tarsus of a 6-year-old, Labrador Retriever with a chronic calcaneal tendon injury and degenerative joint disease. Pantarsal arthrodesis was performed to stabilise the joint and manage the discomfort associated with the condition

Figure 4 (a and b) - Severe hip osteoarthritis in a 6-year-old, German Shepherd Dog. Femoral head and neck ostectomy was performed to relieve clinical signs and improve limb function on the right. The dog regained good limb function and has not yet required further surgery on the contralateral limb

Figure 5 (a and b) - Degenerative change in the hips of a 16-month-old Labradoodle. Total hip arthroplasty was performed to improve this dogs' quality of life due to severe lameness and discomfort during hip manipulation. Significant improvement was seen after surgery



Figure 1



Figure 2a



Figure 2b



Figure 3a







HORIZONTAL BEAM

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HORIZONTAL BEAM

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