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Multimodal Pain Management for Canine Osteoarthritis

Osteoarthritis treatment aims to delay disease progression, decrease inflammation, and ultimately improve the patient's quality of life.

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Osteoarthritis (OA) is one of the most common conditions in dogs, affecting up to 75% of adult medium-size and large dogs.[1-3] One corporate report of OA in dogs estimates a 66% increase in the past decade.[4] Yet a recent study of OA in primary care practices suggested that the prevalence of OA was only 2.5%, and the median age at the time of diagnosis was 10.5 years.[1] This suggests that canine patients are not screened at an early age, owners are not recognizing clinical signs, and veterinarians should be assessing dogs for OA at an earlier age and instituting treatment.

CONSEQUENCES OF OSTEOARTHRITIS

Chronic OA results in pain, lameness, decreased joint range of motion, muscle atrophy, and decreased function and activity. Dogs often become overweight or obese as a result of decreased activity.

IDENTIFICATION OF OSTEOARTHRITIS

Underlying Causes

Canine OA most commonly affects the shoulder, tarsus, and hip. Unfortunately, owners associate OA with old age when, in fact, many cases of OA may be attributed to conditions that develop in dogs younger than 1 year, such as hip dysplasia, elbow dysplasia, and osteochondritis dissecans. Therefore, it is essential for the lifelong health of the dog that veterinarians evaluate large- and giant-breed dogs for these conditions at 6 to 8 months of age. Surgical correction that may slow the progression of OA is often possible if conditions are identified early and appropriate intervention is performed. As patients age, they should be checked during annual evaluations for OA,

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especially of the hips, elbows, and hocks. In addition, cranial cruciate ligament disease may result in secondary OA.

Owner Recognition

Owners should be asked about their dog's ability to function in the home environment (**BOX 1**). Common findings with OA include difficulty rising after rest, difficulty negotiating stairs, reluctance to play, and lameness noted while walking or trotting. Validated questionnaires are available to further quantitate function, such as the Canine Brief Pain Inventory and the Liverpool Osteoarthritis in Dogs. One study found that owners did not recognize clinical signs prior to their dog's OA diagnosis, and some waited months before going to a veterinarian.[5]

BOX 1 Osteoarthritis Screening Questions for Owners

- Does your dog have any difficulty climbing stairs?
- Does your dog have any difficulty descending stairs?
- Does your dog have any difficulty getting up after rest?
- Does your dog have any difficulty moving after rest?
- Does your dog have any difficulty moving after major activity?
- Is your dog less active than when he/she was younger?
- Do you notice your dog limping while walking or trotting, or shifting weight while standing?

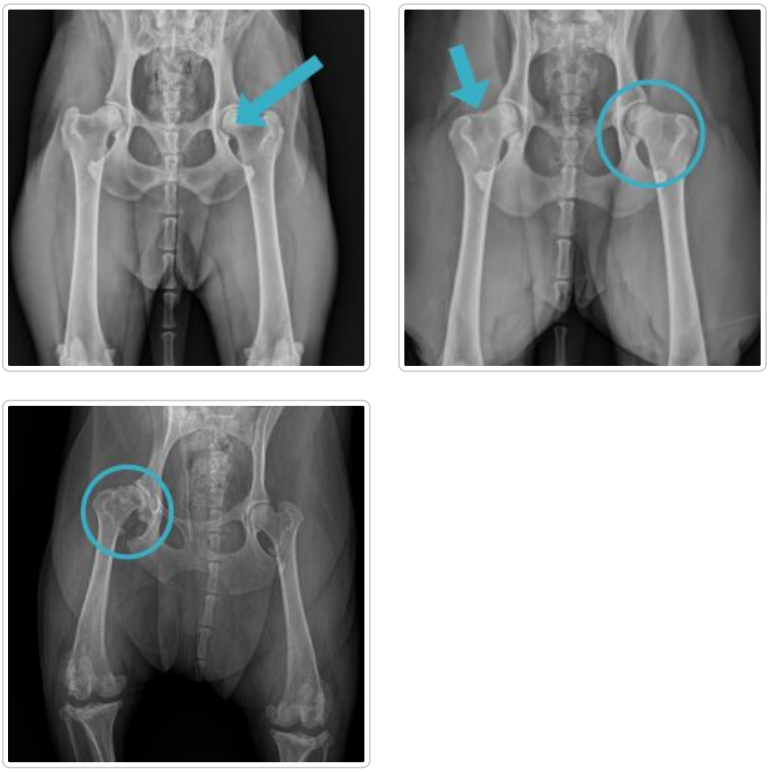
Clinical Assessment

Dogs should be evaluated at a stance, walk, and trot, as well as in a sitting position. Visual assessment of mild lameness is challenging, necessitating careful observation of gait while the dog is walking and trotting in an undistracted straight line. Further evaluation may include having the dog ascend and descend stairs and rise from a sitting position. Even if the gait appears symmetric, a thorough orthopedic examination should be performed because subtle lameness may not be detected. Also, developmental conditions may be bilateral, resulting in symmetric lameness in both limbs.

A thorough orthopedic examination begins with the dog in a standing position to palpate both forelimbs and then both pelvic limbs simultaneously for muscle atrophy and joint effusion. In-depth evaluation of joints may be performed with the dog standing or, preferably, in lateral recumbency. Beginning distally with the toes and proceeding proximally, each joint should be systematically evaluated for periarticular swelling, joint effusion, joint instability, crepitus, range of motion, and pain with manipulation. Muscle mass usually precludes assessment of the hip and shoulder joints for swelling or effusion. Any loss of range of motion or pain at the end of range

generally indicates a problem with the joint.

Radiographs should be taken of joints with suspected OA, but if there are radiographic signs of OA, there are already biochemical or biomechanical changes to cartilage (**FIGURE 1**). Common radiographic findings include subchondral sclerosis of bone, osteophytes, enthesophytes, and joint effusion. Specialized imaging, such as PennHIP for hip dysplasia or computed tomography of elbows, may result in earlier diagnosis of conditions in young dogs.



COMPONENTS OF MULTIMODAL MANAGEMENT

The pathophysiology of OA is complex and involves all components of the joint organ. It is unreasonable to expect that a single treatment will result in optimal improvement. Therefore, a multimodal approach to OA management is crucial to address multiple biochemical pathways and functional deficits.

The traditional management of canine OA includes anti-inflammatory and analgesic medications, disease-modifying OA agents, weight management, exercise modification, physical rehabilitation modalities, environment modifications, and surgical procedures (**TABLE 1**). Managing OA is a lifelong commitment that is focused on decreasing inflammation and disease progression and improving muscle strength and endurance; joint range of motion, performance, and function; and quality of life.

TABLE 1 Sample Treatment Strategies for Osteoarthritis*

OSTEOARTHRITIS (OA) STAGE	FEATURES	EXAMPLES	MAIN GOALS OF TREATMENT	TREATMENT APPROACHES
Early (FIGURE 1A)	Minimal clinical signs, radiographic changes, and functional disability	▪ Dog <1 year old with mild hip dysplasia ▪ Early partial cranial cruciate ligament rupture after tibial plateau leveling osteotomy ▪ 1-year-old dog after surgical treatment of osteochondritis dissecans of the humeral head	▪ Slow OA progression ▪ Maintain as much normal function as possible ▪ Chondroprotection	▪ Weight control ▪ Polysulfated glycosaminoglycans ▪ Nutritional supplements ▪ Consider reparative therapies (e.g., platelet-rich plasma, mesenchymal stem cells) ▪ Regular cardiovascular exercise, including aquatic exercise ▪ Surgical treatment of joint conditions
Moderate (FIGURE 1B)	Moderate clinical signs, radiographic changes, and functional disability	▪ 4-year-old dog with moderate hip dysplasia ▪ Complete cranial cruciate ligament rupture of 3 months' duration before surgical correction	▪ Slow OA progression ▪ Maintain as much normal function as possible ▪ Chondroprotection ▪ Pain management as needed	▪ As for early OA, plus: ▪ NSAIDs for pain and inflammation ▪ Manual therapies, such as stretching and range of motion of joints in affected limbs ▪ Strengthening and joint proprioception exercises ▪ Extracorporeal shock wave treatment ▪ Other physical modalities ▪ **Note:** In these patients, cardiovascular exercise should consist of low-impact exercise
Severe (FIGURE 1C)	Severe clinical signs (e.g., obvious lameness, bunny hopping gait), radiographic changes, and functional disability	▪ Chronic fragmented coronoid process with severe radiographic osteoarthritis, full-thickness cartilage loss, and loss of elbow range of motion ▪ Severe hip dysplasia with pain on hip extension	▪ Maintain best possible function ▪ Pain management	▪ As for moderate OA, plus: ▪ Other pain medications, such as amantadine and gabapentin ▪ Consider intra-articular hyaluronic acid or corticosteroids in place of reparative therapies ▪ Joint replacement surgery if indicated

*Note that not all the treatments listed for each stage of osteoarthritis will be appropriate for all dogs, and overall strategies should be tailored to the individual patient.

Weight Loss

Weight loss can be one of the cheapest and safest methods of treating OA. Noticeable improvement may be seen after loss of 6.9% of body weight.[6] For comparison, it has been suggested that a change of 1 unit on a 9-point body condition score approximates a 5% change in body weight.[7]

Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) are important to reduce pain and inflammation. However, no drug is effective in all dogs, and different NSAIDs have varying effects in different patients, both in efficacy and adverse events. All have shown efficacy in clinical studies. More selective cyclooxygenase (COX)-2 inhibitors, such as deracoxib, firocoxib, and robenacoxib, may have fewer side effects than nonselective COX-2 inhibitors, as suggested by adverse event profiles in clinical studies. Another NSAID, grapiprant, does not inhibit prostaglandin production, but is an EP4 prostaglandin receptor antagonist, and may result in fewer serious adverse events.[8] Still, all NSAIDs have the potential for adverse events, including gastrointestinal, hepatic, and renal effects. The clinical pharmacology of NSAIDs has been reviewed elsewhere.[9]

Dose reduction has been suggested as a means of reducing adverse effects of NSAIDs. This may result in reduced efficacy of the NSAID, as suggested by

one review of dose reduction of meloxicam.[10]

A meta-analysis of adverse events associated with NSAIDs indicated that the most common adverse events included vomiting, diarrhea, and anorexia.[11] Another study evaluated the adverse effects of long-term administration of carprofen, etodolac, and meloxicam for 90 days.[12] Serum gamma-glutamyltransferase activity significantly increased at day 30 in dogs treated with etodolac and meloxicam. Gastric lesions were detected in all dogs treated with etodolac, and 1 of 6 treated with carprofen.

Renal effects of NSAIDs may also be important. Dogs have higher basal levels of COX-2 expression in the kidney than humans. In dogs with chronic kidney disease, COX-2 expression increases and synthesis of prostaglandins shifts to the COX-2 pathway. Therefore, NSAIDs that target COX-2 may adversely affect renal function in dogs with chronic kidney disease.[13]

Other Analgesic Medications

Amantadine is an oral N-methyl-D-aspartate (NMDA) receptor antagonist that may be useful when given with an NSAID.[14] Central sensitization, which may occur with chronic pain, is mediated in part by activation of NMDA receptors. Blocking these receptors may reduce central nervous system hyperresponsiveness, allowing other analgesics to function more effectively. Amantadine may be given on a continual basis if needed, although in some cases it can be given daily for 7 to 14 days and then discontinued until pain worsens. Elimination is almost exclusively via the kidneys, therefore dose reductions should be considered in cases of renal disease. Side effects are rare but can include agitation or diarrhea.

Gabapentin is also sometimes used as an adjunct pain medication for OA; however, its efficacy for acute and chronic pain has been questioned.[15,16] Its best application may be for neuropathic pain. Pregabalin has also been used for OA. Possible side effects may include sedation and weight gain.

Studies have shown tramadol to be ineffective in treating OA. In one study, treatment with tramadol provided no clinical benefit for dogs with OA of the elbow or stifle joint,[17] confirming the results of a prior study.[18]

The use of opioid medications, including codeine preparations, has been suggested in dogs with pain due to OA. One study compared acetaminophen and codeine (1.6 to 2 mg codeine/kg) to carprofen in an acute urate crystal synovitis model.[19] Dogs receiving carprofen had less lameness than those receiving acetaminophen and codeine. Further, oral codeine is not absorbed as well in dogs as in humans.[16]

Nutraceuticals

Many nutritional supplements are available, but consumers should realize that products may not contain what the label indicates. Veterinarians are encouraged to use products that have been tested by independent laboratories. The use of common nutraceuticals has been reviewed elsewhere.[7,20]

Omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are associated with positive effects on OA, demonstrating increased weight bearing and reduction in NSAID dose needed to maintain comfort.[7] In addition, they reduce prostaglandin E2 in cartilage, compete with arachidonic acid in the COX and lipoxygenase pathways, and result in lower levels of inflammatory leukotrienes. Doses of 230 to 370 mg per kilogram of lean body weight$^{(0.75)}$ have been recommended for EPA and DHA.[21] In addition to EPA and DHA supplements, therapeutic diets containing omega-3 fatty acids are also effective. A study of a veterinary therapeutic diet high in omega-3 fatty acids administered to dogs with OA showed significantly higher peak vertical forces after 13 weeks compared with baseline and dogs fed the control diet.[22]

Green-lipped mussel has also shown to have benefit in dogs with OA.[7] It also contains omega-3 fatty acids, but there may be other mechanisms of action, including modulation of chondrocyte activity and anti-inflammatory effects.

Avocado/soybean unsaponifiables have anabolic, anticatabolic, and anti-inflammatory effects on chondrocytes.[23] They may increase transforming growth factor-β and collagen and aggrecan synthesis while inhibiting nuclear factor kappa B (NF-κB) activation, interleukin (IL)-1β–induced collagenase, matrix metalloproteinase activity, nitric oxide, and prostaglandin E2.

Undenatured type II collagen (UC-II) is a relatively new nutraceutical.[24] One study showed that daily treatment of arthritic dogs with UC alleviated arthritis-associated pain and lameness. These effects were noted when UC was given alone or in combination with glucosamine and chondroitin, although the results were better when administered alone.[25]

Glucosamine and chondroitin are commonly used, but data on appropriate dose and efficacy are scarce.[26] Nevertheless, in one survey, veterinarians recommended using glucosamine/chondroitin products and omega-3 fatty acids more often than other products for their patients and their own pets.[27] One recent study indicated that glucosamine and chondroitin administered for 70 days resulted in improvements in subjective scores for pain, weight bearing, and overall condition from pretreatment values.[28] Other studies have shown little or no effect.

Boswellia is purported to inhibit 5-lipoxygenase and matrix metalloproteinases and to decrease tumor necrosis factor and IL-1β. Boswellia was evaluated in 24 dogs in a multicenter study, with improved

lameness and pain noted in 17 dogs.[29] However, this study was not randomized or placebo-controlled.

Polysulfated Glycosaminoglycans

Polysulfated glycosaminoglycans (PSGAGs) are disease-modifying osteoarthritis drugs that are anti-inflammatory, inhibit matrix metalloproteinases within the joint, and have a positive effect on hyaluronic acid (HA) and glycosaminoglycan synthesis in diseased joints. PSGAGs have many beneficial mechanisms and are generally effective in improving lameness,[30,31] but they must be administered by injection.

Intra-articular Treatments

Intra-articular treatments have increased in popularity. HA, platelet-rich plasma (PRP), mesenchymal stem cells (MSC), and corticosteroids are possible intra-articular therapies.

MSC therapy for dogs with OA has been recently reviewed.[32] Five studies demonstrated improved pain, range of motion, and visual analogue scale scores in dogs treated with adipose-derived MSC, MSC plus PRP, MSC plus HA, or stromal vascular fraction. One study suggested better results with MSC than with PRP 6 months after treatment. Improvement persisted for 3 to 6 months. Future studies should evaluate MSC with placebo controls and multiple intra-articular injections in combination with other therapies, such as PRP or HA.

One study compared intra-articular treatment with HA, triamcinolone, and PRP in dogs with hip dysplasia.[33] Improvement in several validated questionnaires and weight bearing at a stance had longer duration of effect for dogs treated with HA and PRP, while triamcinolone had the greatest effect on pain improvement (95% improvement over controls). Dogs treated with PRP and HA had 57% to 81% improvement in functional evaluation and impairments due to OA. Other studies also support the use of PRP for OA.[34,35]

Physical Rehabilitation

Exercise

Exercise is recommended as one of the main treatments for OA in people, and anecdotal observations suggest that it is useful in dogs. A recent review of human literature found that 90% of articles regarding exercise-induced analgesia demonstrated positive effects of exercise, and analgesia was demonstrated with running, swimming, and resistance training.[36] Although specific studies of the amount and type of exercise do not yet exist in dogs, low-impact, regular exercise titrated to the dog's ability is logical. If appropriate, the amount of increase in weekly low-impact exercise may be up

to 5% to 10% in dogs with severe OA, as long as the dog does not worsen with increased activity. Underwater treadmill walking is appropriate for dogs with OA due to the buoyancy, resistance, and hydrostatic pressure provided by water. Caution should be used with swimming for severely affected dogs because the joints move rapidly during swimming; underwater treadmill walking allows controlled velocity and simulates more normal joint flexion and extension.

Thermal Modalities

Cold decreases blood flow, inflammation, hemorrhage, and metabolic rate.[37] Studies of cryotherapy and OA suggest positive benefits, including less stiffness and pain and improved joint range of motion.

Heat increases blood flow and tissue extensibility and may decrease pain, muscle spasm, and joint stiffness.[37] Heat is contraindicated if swelling or edema are present and may increase inflammation.

Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy (ESWT) is the transmission of high-pressure acoustic waves through tissues to a target area, where energy is released and a variety of growth factors are produced. Studies of ESWT for OA have shown positive benefits with increases in ground reaction forces.[38,39]

Transcutaneous Electrical Nerve Stimulation

Transcutaneous electrical nerve stimulation (TENS) provides analgesia through several mechanisms of action, including the “gate theory” of pain control.[40] A single TENS treatment in dogs with stifle OA can result in significantly improved weight bearing. While daily application is likely necessary, it may give added benefit to medications and may be used in patients that cannot tolerate certain medications.

Therapeutic Laser

Therapeutic laser (TL) treatment affects intracellular photochemical reactions. Results of TL in patients with OA have been mixed. One study in dogs with elbow OA treated with 10 to 20 J/cm^2 of TL or a placebo to both elbows for 6 weeks showed a reduction in NSAID dose and lameness scores in TL-treated dogs.[41] Another study of TL using 10 J/cm^2 versus placebo failed to show an improvement in ground reaction forces in dogs with hip or stifle OA.[42]

If TL is used, the hair should be clipped to improve transmission of photons to target tissues, and consideration should be given to the color of the skin and the depth of the tissues.[43,44]

Surgical Treatments

Many surgical procedures have evolved to help manage OA, including total hip, stifle, and elbow replacement. Procedures for severe medial compartment disease of the elbow secondary to fragmented medial coronoid process include ulnar osteotomy, proximal abducting ulnar osteotomy, sliding humeral osteotomy, and the canine unicompartmental elbow implant. Arthrodesis may also be a choice with severe carpal or tarsal OA.

Environmental Modifications

Altering the environment may be helpful for arthritic dogs. A soft, well-padded bed should be provided, along with good flooring to prevent slips and falls. Owners can minimize stair climbing through the use of fixed ramps. Portable ramps are available to assist dogs with getting in and out of vehicles. Additional harnesses and support devices are also available. Owners should avoid overdoing activities and prevent excessive play with other pets.

Other Treatments

Other potential treatments for OA include acupuncture, chiropractic, massage, pulsed electromagnetic field therapy, prolotherapy, joint mobilization and manipulation, radiation therapy,[45] and nuclear magnetic resonance treatment.[46,47]

CONCLUSION

OA is common in dogs. Management involves multiple modalities and must be tailored to each patient and its owner. Weight control, medications, joint supplements, and physical rehabilitation are the main components of OA management. When selecting treatments, veterinarians should consider the efficacy, safety profile, mechanism of action, and patient response for each. Although not all dogs respond equally to all treatments, cooperation among all parties is vital to carry out an appropriate management program, and monitoring is essential to help with decision-making for further treatment.

References

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