CLINICAL NOTES: Multimodal Pain Management for Dogs and Cats

Osteoarthritis (OA) is a complex disease that affects 1 in 5 adult dogs presented to veterinary practices. Because no single strategy can provide complete therapy, combining various modalities may result in synergistic effects, minimize drug doses, and reduce the likelihood of adverse effects.

MANAGEMENT OF OSTEOARTHRITIS

Since many patients will have nonsteroidal antiinflammatory drugs (NSAIDs) prescribed, a CBC, serum biochemistry profile, and urinalysis (UA) to establish baseline values and detect any possible contraindications should be added to a thorough workup of the patient. Devoting adequate time to explain the disease process and patient care plan to the client is important in improving compliance. Veterinarians must impress on owners that the management of chronic OA is a lifelong commitment and is hard work.

Antiinflammatory Agents

Nonsteroidal antiinflammatory agents (NSAIDs) provide rapid control of OA pain and inflammation and are the cornerstone of therapy. Not all patients respond in the same fashion to every NSAID. Thus, veterinarians may wish to evaluate different NSAIDs for efficacy and adverse events in a particular patient. A 2-week trial is generally sufficient, which should be followed by a wash-out period of several days before trying another NSAID. Titrating to the minimum effective dose may reduce adverse effects.

Carprofen, etodolac, deracoxib, meloxicam, and firocoxib are approved for the management of OA in dogs. The newest available NSAID, robenacoxib, is approved for postoperative analgesia in cats. Although robenacoxib is not approved for chronic pain in cats and dogs in the United States, it is approved for such use in other countries and may be useful.

Other Analgesic Agents

Chronic pain may become “resistant” to treatment with NSAIDs, necessitating the addition of other analgesic agents. Among the choices for adjunctive treatment are:

- Amantadine, the most commonly used oral NMDA (N-methyl-D-aspartate) receptor antagonist
- Gabapentin, which may be involved in postsynaptic neuron firing
- Amitriptyline, a tricyclic antidepressant that has been used as an adjunct to other analgesics for chronic pain
- Opioids that may be used for short-term "rescue" analgesia or when other medications are no longer effective. Oral codeine, a mu agonist, has been used in combination with acetaminophen. This combination should NOT be used in cats due to the risk of fatal methemoglobinemia.
- Tramadol, a mu agonist with monoamine-oxidase (MAO) reuptake inhibitor properties, which may be used alone or combined with other analgesics (NSAIDs, mu agonists) to enhance its efficacy. However, such combinations may also increase the incidence of adverse events. There is little safety or efficacy data on tramadol in dogs and cats.

Slow-Acting Disease-Modifying Osteoarthritic Agents

Slow-acting disease modifying agents such as Adequan help to slow the progression of disease and preserve remaining cartilage, so adding them early in the dis-
ease can be highly beneficial. Polysulfated glycosaminoglycan (PSGAG) is antiinflammatory, inhibits destructive enzymes, and has a positive effect on hyaluronic acid and GAG synthesis. Some patients may benefit from periodic administration of intraarticular injection of HA.

Nutritional Management of Osteoarthritis

Obesity is strongly associated with the development and progression of OA in dogs. Therefore, nutritional management is a key component of arthritis management. Body condition scores (BCSs) should be emphasized and interpreted the same way as laboratory values; a specific prescription of weight loss strategies should be developed for each patient.

Commercially available diets have been clinically effective in patients with OA. Hill’s Prescription Diet j/d Canine Mobility is a diet for patients with OA with four grade 1 studies to show its clinical effects.

Other nutraceuticals include

- Certain polyunsaturated fatty acids (PUFAs), especially omega-3 fatty acids
- Glucosamine and chondroitin sulfate
- Avocado-soybean unsaponifiables (ASU), which stimulate cartilage matrix production and reduce destructive enzymes in tissue culture
- S-adenosyl-L-methionine (SAMe), which is involved in cell proliferation, protein synthesis, and free-radical scavenging and has antiinflammatory and analgesic properties. SAMe also enhances proteoglycan synthesis and secretion in vitro.

Efficacy in animals with OA has not been established for these agents.

Hyperimmune Milk Protein

Hyperimmune milk (Duralactin®) is produced by cows that are immunized with intestinal bacterial antigens, resulting in high-molecular-weight immunoglobulins (IgG) and antiinflammatory low-molecular-weight components. These components may inhibit inflammation by interfering with neutrophil migration from the vascular space. In fact, in vivo studies have demonstrated that this compound suppressed neutrophil migration by up to 75%. A follow-up study demonstrated the formation and maintenance of vascular tight junctions on exposure to the antiinflammatory components of hyperimmune milk. The formation and maintenance of vascular tight junctions upon exposure to hyperimmune milk protein may restrict the extravasation of neutrophils through vascular cell junctions, resulting in antiinflammatory action.

The addition of hyperimmune milk protein to the diet of human patients with either OA or rheumatoid arthritis was found to considerably relieve their painful clinical signs. In a survey of over 8,000 human patients with OA, 80.2% of respondents reported considerable improvement in joint pain with hyperimmune milk and 72.0% reported improvement in morning stiffness. In an 8-week randomized, controlled trial of dogs with musculoskeletal impairment, 1 gram twice a day Duralactin was more efficient than placebo in improving function as assessed by a questionnaire addressed to pet owners.

Exercise

Exercise is a vital component of OA treatment, both to help with weight loss and to maintain muscle mass and soft tissue support. Acute exercise increases the resting metabolic rate for 2 to 48 hours, and frequent exercise over an extended period may prevent the reduced resting metabolic rate associated with caloric restriction. Therapeutic exercise also increases muscle mass, making it easier to burn calories.

Physical Modalities Used in Osteoarthritis

Among physical modalities that may be beneficial to patients with OA are cryotherapy, therapeutic ultrasound, therapeutic laser, and extracorporeal shock waves, which have been successfully used in OA.

Sample Protocol for Osteoarthritis Treatment

1. Blood analysis/UA before NSAID commencement to establish baseline/safety
2. Day 1
   - BCS & diet discussion
   - NSAID
   - Hill’s Prescription Diet j/d Canine Mobility
   - Adequan
   - Duralactin +/- other nutraceuticals
   - Weight loss (choose Hill’s j/d or Metabolic instead of j/d if pet is obese)
   - +/- Adjunctive drug for pain
   - Exercise/rehabilitation/physical modality recommendations
3. 14-day recheck
   - Blood analysis to determine NSAID safety
   - BCS & diet discussion
   - Continue Duralactin +/- other nutraceuticals, Adequan
   - Adjust/eliminate adjunct medications
   - Discuss exercise/rehabilitation/physical modalities
4. 30-day recheck
   - BCS & diet discussion; change to Hill’s j/d if obese patient has attained ideal weight
   - Decrease/eliminate NSAID
   - Continue Duralactin +/- other nutraceuticals, Adequan
   - Adjust/eliminate adjunct medications
   - Discuss exercise/rehabilitation/physical modalities
5. 60-day recheck
   - By telephone or in clinic
   - BCS & diet discussion
   - Further reduction/elimination of NSAID?
   - Continue Duralactin +/- other nutraceuticals, Adequan
   - Discuss exercise/rehabilitation/physical modalities
6. 6-month recheck
   - BCS & diet discussion; dog/cat should be on Hill’s j/d at this point
   - Blood analysis/UA for NSAID maintenance if still on NSAID
   - Continue Duralactin +/- other nutraceuticals, Adequan
   - Discuss exercise
7. Continue 6-monthly rechecks as above, or at any other time that owner has concerns