Zoledronic Acid for Canine Osteoarthritis

The bisphosphonate group is a drug class evaluated and used for its modulatory effects on bone. Bisphosphonates reduce bone resorption by acting on recruitment, activity, or life span of osteoclasts. This study investigated the effects of zoledronic acid on preservation of subchondral bone in an experimental model of cranial cruciate ligament (CrCL) disease.

The left CrCL was surgically transected in adult dogs (n = 21). Dogs were stratified into 3 equal groups: control, low-dose zoledronic acid (10 µg/kg), and high-dose zoledronic acid (25 µg/kg). Injections were given q3mo SC for 1 year. Biochemical markers of collagen synthesis and destruction, bone-specific ALP, and indicators of cartilage turnover were measured at intervals over 12 months. Animals were euthanized, and necropsies were performed after 1 year.

Zoledronic acid was found to provide chondroprotective effects on articular cartilage, quantified as a combination of macroscopic and biochemical changes on samples obtained 1 year after CrCL transection. The protective effect was identified primarily as a reduced number of cartilage lesions in the high-dose group. Effects may have been partially mediated by regulation of collagenase activity, as types I and II collagen concentrations were significantly reduced in synovial fluid from bisphosphonate-treated dogs. Osteophyte count was not affected by zoledronic acid; therefore, radiographic osteoarthritis (OA) scores did not reflect chondroprotective drug benefits.

Supported in part by a grant from Novartis Animal Health

Commentary

Zoledronic acid (zoledronate) is a newer-generation bisphosphonate that is expensive, but safe and relatively easy to use. The drug is under investigation as a palliative measure in dogs with appendicular osteosarcoma that are not candidates for limb amputation[1,2] and is anecdotally given as an adjunctive measure to patients undergoing CyberKnife radiation as a limb-sparing procedure. Based on study results, zoledronic acid may also be useful in OA cases. Because the chondroprotective effects supposedly took months to occur and the experimental model was an acute insult (no prior history of OA), it is unclear which animals with OA would benefit from the treatment (eg, the dog with CrCL rupture undergoing surgery or the 12-year-old Labrador retriever with multifocal OA and joint derangement). It is also unclear whether the drug provided pain relief or improved joint function. Zoledronate has been shown to cause osteomalacia of the jaw with chronic use in humans with cancer, so further studies regarding long-term use are warranted in animals.—*Heather Troyer, DVM, DABVP, CVA*

Source

Chondroprotective effects of zoledronic acid on articular cartilage in dogs with experimentally induced osteoarthritis. Dearmin MG, Trumble TN, García AP, et al. *AM J VET RES* 75:329-337, 2014.

1. **Zoledronic acid for the treatment of appendicular osteosarcoma in a dog.** Spugnini EP, Vincenzi B, Caruso G, et al. *J Small Anim Pract* 50:44-46, 2009.
2. **Effect of zoledronic acid and amputation on bone invasion and lung metastasis of canine osteosarcoma in nude mice.** Wolfe TD, Pillai SP, Hildreth BE 3rd, et al. *Clin Exp Metastasis* 28:377-389, 2011.

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