



Pain Management Strategies for Chronic Osteoarthritis in Dogs

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Osteoarthritis

- AKA degenerative arthritis or degenerative joint disease
 - Characterized by pain and lameness
 - Associated with pathological changes in the tissues of synovial joints including loss of articular cartilage
- 20% of dogs over 1 year of age are affected
- A group of mechanical abnormalities involving degradation of joints
 - Hereditary
 - Developmental
 - Metabolic
 - Mechanical



Osteoarthritis

- Joints affected
 - Hips, elbows, stifles, vertebral facets, carpal joints, tarsal joint, metacarpal and metatarsal joints, etc...
- Large breed dogs most common
 - Smaller breeds are becoming more recognized
- Not part of the normal aging process
- Instability, incongruity, uneven load-bearing, previous injury predispose to OA
 - Abnormal stress and chronic inflammation of intraarticular cartilage

Osteoarthritis

- Pathology
 - Loss of cartilage
 - Bone surface exposure
- Decreased movement secondary to pain
- Regional muscle atrophy
- Ligaments laxity
- Water content of the cartilage decreases as a result of a reduced proteoglycan content
 - Cartilage becomes less resilient
 - Collagen fibers of the cartilage become susceptible to degradation
 - breakdown products from the cartilage are released into the synovial space and cause inflammation
 - Osteophytes may form on margins in an attempt to improve congruency of cartilage



Pain Assessment

- Animals with OA learn to compensate gait and movement to reduce OA pain
 - Develop myofascial pain
- Systemic approach to muscle palpation and limb extension and flexion
- Some will carry tension in cervical and masticatory muscles
- Palpate for tenderness and hardness
- Weight distribution
- Owner assessment before and after therapy



Pain Management Options

- Pharmacologic
 - Systemic
 - Intraarticular
- Nutritional Supplements
- Physical modalities
- Weight loss
- Complimentary modalities



Systemic Pharmaceuticals

- NSAIDs
- Opioids
- NMDA antagonists
- Gabapentin
- PSGAG
- Hyaluronan

NASIDs

- Most frequently recommended treatment of OA
- Effective
 - Analgesic
 - Anti-inflammatory
- Easy administration
- Profitable
- Narrow therapeutic/toxic margin
 - Side effects can be catastrophic



NSAIDs

- Approved for veterinary use
 - Ketapofen
 - Etodolac
 - Carprofen
 - Deracoxib
 - Firocoxib
 - Meloxicam
- Side effects
 - Gastrointestinal upset and lesions
 - Renal injury
 - Hepatic injury
 - Coagulopathy
 - Impairment of bone healing

NSAIDs

- Used with close monitoring
 - Serial serum chemistries
 - BUN
 - Creatinine
 - Liver enzymes
 - Owner monitoring
 - Decreased appetite
 - Diarrhea
 - Dark stool
 - Vomiting

Opioids

- Most opioids work through central opioid receptors that activate/enhance descending pain modulating tracts
- Most are available in parenteral formulations that make dispensing difficult
- Most oral formulations have minimal/variable GI absorption
 - Methadone
 - >70% bioavailable in humans
 - Almost 0% bioavailable in dogs
 - Similar with other oral opioids
 - Tramadol and tapentadol may be exception

Tramadol

- Centrally acting synthetic opioid
 - Mode of action not completely understood
 - Parent compound has low affinity to μ receptor
 - O-demethylated metabolite M1 has higher affinity
 - 6 times more potent analgesic
 - 200 times more potent binding to μ receptor
 - Weak inhibition of re-uptake of norepinephrine and serotonin
 - Analgesic effect may be independent of opioid action



Tramadol

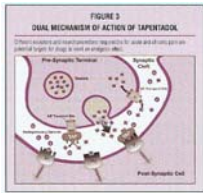
- Pharmacokinetics
 - Bioavailability of 65%
 - Dogs tend to not make M1
- Efficacy studies
 - Questionable value
 - May not provide any analgesia
- Pronounced effect in cats
 - Euphoria, dilated pupils, sedation
 - 1 mg/kg SC did not produce thermal or mechanical antinociception

Tramadol

- Indicated for mild to moderate pain
- Does not seem to induce tolerance
 - Non-opioid mechanisms?
- Best suited for use in combination with other analgesics
 - NSAID's
- Avoid use with MAOs or SSRIs
 - serotonin syndrome?



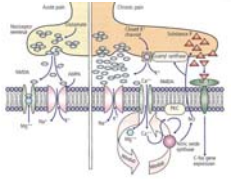
Tapentadol



- Similar to M1 metabolite of tramadol in structure
- MOP receptor agonist and norepinephrine reuptake inhibitor
- Very potent analgesic
 - Does not require metabolism for activation
 - Rapid oral absorption in dogs (but lower bioavailability than in other species)
 - Half-life of 4 hours

NMDA Antagonists

- Located in the dorsal horn of the spinal cord
- Activation of these receptors is associated with chronic pain
- Chronic stimulation of $\alpha\delta$ and c nerve fibers
 - Release of glutamate
 - Glutamate activated NMDA receptors
 - Allows transmission of ascending pain impulses



Amantadine

- Antiviral drug
- NMDA antagonist activity in spinal cord
- Allodynia and opioid tolerance
 - Chronic pain
 - Lowering of opioid doses
- Neuropathic pain in combination with opioids
- Dosages
 - 3-5 mg/kg PO q24h
 - Behavioral changes occur at doses greater than 15 mg/kg
 - Toxic dose in cat is 30 mg/kg



Oral Ketamine

- NMDA antagonist
- Useful in chronic pain conditions
- 0.3 mg/kg once daily in gelatin cubes
 - -Dr. Michael Tomasic
- Recipe:
 - 1 gram ketamine in 100 ml 12% gelatin solution
 - Add beef/chicken/vegetable bullion and salt for palatability
 - Once gelatin has set, cut into appropriate sized cubes for daily dosing

Memantine

- Novel class of Alzheimer's Disease medications
 - First synthesized in 1968
 - Efficacy for Alzheimer's is unknown
- Acts on glutamatergic system by blocking NMDA receptors
 - Effective for chronic pain
- Dose of 0.1 mg/kg PO once daily

Gabapentin

- Influences central nervous system and is recognized as being beneficial for the treatment of neurogenic and chronic pain
- Therapeutic action is believed to involve voltage-gated N-type calcium ion channels
- Reduces allodynia and hyperalgesia
- Dosages
 - Dogs: 2-20 mg/kg PO BID to QID
 - Cats: 2-5 mg/kg PO BID



Polysulfated Glycosaminoglycan

- Approved for use in dogs as a disease modifying agent of OA
- 5 mg/kg IM twice weekly for 4 weeks
- Research shows PSGAG inhibits cartilage matrix degradation
- May reduce lameness in dogs with OA
- Analogue of heparin and should not be used in animals with bleeding disorders



Hyaluronan

- Nonsulfated glycosaminoglycan
 - Major component of synovial fluid
- No product approved for use in dogs
- Equine produce labeled for IV and intraarticular injection
- Canine studies
 - No clinical improvement or preventative effects identified
 - No influence on synovial fluid parameters



Intraarticular Pharmaceuticals

- Intraarticular medications provide for targeted therapy and reduced doses
 - Minimized systemic side effects
 - Requires sedation/anesthesia for injection
- Medications most commonly used:
 - Opioids
 - Corticosteroids

Intraarticular Opioids

- Morphine most commonly used
 - Longest resident time
 - Use preservative free preparations
- μ opioid receptors have been identified in articular tissue of rats, cats, dogs, horses, and humans
 - Synovial membrane, bone marrow, periosteum, juxta-articular bone, cartilage, and chondrocytes
 - decreases numbers of inflammatory cells



Intraarticular Corticosteroids

- Triamcinolone
 - Reduces the formation of osteophytes in an OA model in dogs
 - Reduced severity of cartilage lesions and numbers of inflammatory cells
- However,
 - Recent studies indicate possibility of corticosteroid toxicity to chondrocytes and long term may induce crystal arthritis
- Use for chronic OA in dogs can not be recommended at this time

Nutritional Supplements

- Many nutritional supplements are available with claims to help alleviate clinical signs of arthritis
 - Minimal evidence to back up claims
- Chondroitin sulfate and glucosamine
- Green-lipped mussel preparations
- Omega-3(n-3) fatty acid diet supplements
- Alenza

Chondroitin Sulfate and Glucosamine

- Structural component of cartilage
 - Provides resistance to compression
- No significant side effects from overdoses or long term use have been identified
 - Considered one of the safest options for OA
- Mechanisms of action
 - Anti-inflammatory
 - Stimulation of synthesis of proteoglycans and hyaluronic acid
 - Decreases catabolic activity of chondrocytes
 - Reduced IL-1 β -induced nuclear factor- κ B
 - Positive effect on OA structural changes in subchondral bone



Green-Lipped Mussels

- Cultivated mollusc in New Zealand
- Unique combination of fatty acids not found in any other marine or plant life
 - Polysaccharides and glycosaminoglycan
 - Inhibits 5-lipoxygenase
 - Anti-inflammatory
- Studies in dogs suggested mild to moderate improvement
 - Quality of studies are questionable
- Difficult to recommend at this time without further evidence based studies



Omega-3(n-3) Fatty Acid

- Advocated as an adjunctive therapy for OA
- Polyunsaturated fatty acids (PUFA) are incorporated into cell membrane phospholipids
 - Dependent on diet
 - Arachidonic acid is predominant PUFA in cell membranes
 - Converted into inflammatory prostaglandins
 - Diets high in Omega-3s result in increased eicosapentaenoic acid
 - Competes with AA as a substrate for COX enzyme
 - Produced less inflammatory prostaglandins
- One study showed improvement in OA after 90 days feeding trial



Alenza

- “Multi-system support for whole body comfort in aging and active dogs”
- Chewable tablet
 - Vexadol™
 - Naturally occurring bioflavonoids
 - Baicalin from Scutellaria baicalensis
 - Catechin from Acacia catechu
 - Boswellia serrata
 - Antioxidants (Vit C, selenium, Vit E)



Physical Modalities

- Use of physical rehabilitation methods
 - Heat, cold, water, sound, electricity, massage, and exercise
- May increase blood and lymph flow, resolve inflammation, minimize muscle atrophy and fibrosis, and provide positive psychological effects for patients and owners
- Cryotherapy
 - Heat
 - Passive range-of-motion
 - Stretching
 - Massage therapy
 - Therapeutic ultrasound
 - Laser
 - Electrical stimulation
 - Active exercise

Cryotherapy



- “Local hypothermia:
 - Used for acute inflammation
 - Promotes vasoconstriction
 - Limits blood flow
 - Reduced edema
 - Skeletal muscle relaxation
 - Improves venous return and prevents endothelial damage
 - Decreased nerve conduction
 - Mild analgesia
- Penetrated to a tissue depth of 1 to 4 cm
 - Greatest temperature change at 1 cm
- No longer than 30 minutes 2 to 4 times daily

Heat



- Moist heat
 - Typically used in chronic OA cases
 - Not for use with acute inflammation
 - Use prior to:
 - Stretching, massage, range-of-motion, or active exercise
 - Reduces muscle spasm and increased blood flow
- Superficial heat
 - Reaches tissue depth of 1 to 2 cm
 - Vasodilation
 - Mild sedation
 - Reduces muscle pain
 - Increases compliance of joint capsules and connective tissue
- Hot packs, warm baths, warm towels
 - 15 to 20 minutes 2 to 3 times daily
 - No warmer than 104 to 109° F

Passive Range-of-Motion

- Helps to restore joint motion
- Advance joint through comfortable range of motion
 - Patient should not experience discomfort or pain
 - Can lead to reflex inhibition, limited use of limb, fibrosis, and delayed return to use
 - Can administer analgesics prior
- Joint is moved without effort from the patient
 - Maintain normal range
 - Prevent contracture
 - Improves blood and lymph flow
 - Stimulates sensory awareness
 - Reduces catabolic effect on cartilage
- 10 to 15 repetitions two to three times daily



Stretching

- Increase tissue extensibility and reduce muscle contracture from disuse
- Performed several times daily
 - Especially after application of heat or ultrasound
 - Muscles are stretched and held for 10 to 30 seconds
 - Repeated 10 times per session



Massage Therapy

- Usually combined with other techniques
- Increases blood and lymph flow
- Breaks down adhesions
- Muscle relaxation
- Analgesia
- No effect on muscle mass, strength or atrophy
- 5 components of massage
 - Rhythm
 - Rate
 - Pressure
 - Direction
 - frequency



Therapeutic Ultrasound

- Used for heating deeper tissues
- Helps control pain and improve tissue motion
- Sound waves are converted heat as they are absorbed
 - Stimulates fibroblast activity, improves circulation, increases strength and pliability of tendons
- Depth of 5 cm can be reached
 - Elevated temperature to 104 to 113° F
 - 1 MHz – 3 to 5 cm depth
 - 3 MHz – superficial penetration
 - Used 2 to 3 times weekly



Laser

- Red and near-infrared light may help to reduce pain and inflammation
- May help control pain of OA
- Laser probe held directly of painful area



Electrical Stimulation

- Used to increase muscle strength, improve range of motion, re-educate muscles, decrease edema and pain
- Biphasic or monophasic pulse
- Transcutaneous electrical nerve stimulation (TENS)
- Treatments of 20 to 30 minutes



Active Exercise

- Improved muscular strength and coordination
- Cardiovascular endurance and function
- Reduces joint stiffness and muscle atrophy
- Aids in control of body weight
- Periodic cartilage loading
 - Increases metabolism and proteoglycan synthesis
- Low impact preferred
 - Leash walking
 - Treadmill
 - Water treadmill
 - swimming



Weight Loss

- For overweight animals, can be one of the most important aspects of management program
- Link between obesity and OA is well established in man
- Dogs
 - Preventing the development of overweight and obesity reduces prevalence of hip dysplasia and OA
 - Weight loss is an effective treatment in OA in affected overweight and obese dogs



Complimentary Modalities

- Acupuncture
- Herbal therapy
- Agility training
- Chiropractic



Conclusions

- Osteoarthritis is an insidious condition that can limit mobility, cause pain, and reduce quality of life
 - Owners may elect euthanasia of animals that can be successfully managed
 - Veterinarians should be familiar with available options to offer to their clients and patients
- Medications, physical medicine, and diet changes can make a substantial difference



Questions?
