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
  - Ketoprofen
  - Etofenac
  - 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 formulation 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 αδ 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 cannot 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-1β-induced nuclear factor-κB
  - 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 edema
    - 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?