OSTEOARTHRITIS (OA) – DOES ANY TREATMENT REALLY WORK?

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Introduction

Osteoarthritis remains a disease that we can at best hope to control rather than cure. Control in this context refers to both the control of the clinical signs of OA and control of this chronic, progressive, debilitative condition.

Given the above, the following list of aims of treatment of OA in dogs and cats is appropriate:

• provide pain relief
• improve quality of life
• be well tolerated (incl long term)
• decrease inflammation
• decrease rate of joint damage
• easy tailoring of dose to body wt

Surgery plays an important part in the overall management of OA, but major benefits of surgery are seen only in a number of select groups of arthritic patients:

• to address gross joint instability (eg ligamentous injury)
• to remove bone fragments and/or cartilage flaps and address the cartilage defect
• corrective osteotomy to alter load bearing
• salvage procedures for end-stage joint pathology.

This leaves a very large group of arthritic patients for which surgery will not offer much hope of benefit, and for these patients non-surgical management will remain the mainstay of achieving the goals of pain relief and improved quality of life.
Treatment modalities for OA include dietary manipulation, physical therapy and surgery as well as four distinct groups of agents - non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, disease-modifying osteoarthritic drugs (DMOADs) and nutraceuticals. A fifth group of pain-modulating modalities is gathering widespread support in certain countries.

**Therapeutic agents in the management of OA**

1. **Non-steroidal anti-inflammatory drugs (NSAIDs)**
   
   NSAIDs remain the first line of approach for many veterinarians treating dogs with OA. Historically, the choice of drug has been very much a matter of personal preference. The incidence of side effects such as gastrointestinal bleeding is variable and occurs mainly in dogs on higher dose rates. Some NSAIDs have the potential to exacerbate OA through inhibition of proteoglycan synthesis in cartilage. In addition, by relieving pain, they may permit greater use of the damaged joint and therefore increase wear and tear.

   Fortunately as veterinarians we now have the choice of a number of effective NSAIDs registered for use in dogs which should have reduced incidence of side effects, thus allowing safer long-term therapy, which of course is desirable in the management of a chronic progressive disease such as OA. However, it is important to recognise that the potential for serious side effects remains, and the owners of all patients on NSAID therapy should be informed about this risk and advised to contact their veterinarian if signs such as inappetance, lethargy, vomiting or diarrhoea are seen.

   Finally, be aware of the greatly increased chance of side effects when NSAID therapy is combined with corticosteroid therapy. This combination should be avoided.

   The concept of tailoring NSAID dosage to the pattern of activity of the patient has been used by some veterinarians to help reduce the potential for side effects and to decrease the total cost of long term therapy. This concept takes into account that for many older arthritic animals owned by people who work long hours, the weekdays (Monday to Friday) are spent lying around doing very little and activity such as walks, playing etc occur only sporadically. For these patients, administration of NSAIDs can be limited to the days around a known period of activity (eg Friday to Monday if weekend activity is the usual pattern) with a break from therapy during the weekdays. However, this form of therapy is not compatible with our understanding of the role of regular exercise in the overall management of joint disease (see below under physical therapy) so pulse dosing should only be used when a regular daily exercise program cannot be instituted.

2. **Disease modifying osteoarthritic drugs (DMOADs):**

   The theories on the aetiopathogenesis of OA all concur that the abnormal loading of articular cartilage (through a variety of postulated mechanisms) is a crucial step in the development of OA. The fact that a net loss of cartilage proteoglycan occurs reflects the fact that the ability of the chondrocytes to manufacture new matrix components is unable to keep pace with the rate at which the matrix is being degraded. This is despite the fact that the chondrocytes are metabolically hyperactive especially in the early stages of OA.

   It has been suggested therefore that a rational approach to drug therapy in OA is to perfuse cartilage with
molecules that slow down the degradative processes and support the biosynthetic functions of the chondrocyte. In addition, the therapeutic agent should promote the synthesis of macromolecular hyaluronic acid, decrease synovial inflammation (if present) and relieve pain. Such an agent would be acting to preserve the cartilage and therefore could be termed “chondroprotective”.

Although “chondroprotective drugs” was the original term coined to describe this new group of agents, further study has shown that some of these agents may have other effects apart from those acting to preserve/restore cartilage matrix. To take account of this, a new classification of therapeutic agents has now been developed - Disease Modifying Osteoarthritic Drugs(DMOADs)

The drugs formerly referred to as chondroprotective are now are included in the DMOADs.

The two products that fit this category are polysulfated glycosaminoglycan (usual trade name “Adequan”), and pentosan polysulfate (usual trade name Pentosan or Cartrophen). They are variably registered and available in different countries. There are few publications of controlled studies to assess the efficacy of these products, but the results of these studies tend to support a reduction in clinical signs of OA associated with their use at recommended doses/ regimes.

3. Nutraceuticals (oral glucosamine/chondroitin sulfate/green lipped muscle extract etc)

These products are representative of a group of products that appeared on the veterinary market around 10 years ago, close on the heels of their entry into the human health market. They are referred to as ‘nutraceuticals’, indicating their place as somewhere between a nutritional supplement and a pharmaceutical agent. Many additional products have entered the market over the past few years, accompanied by claims regarding the benefit of these products and backed by scientific argument, which emphasizes the role of the various components in connective tissue metabolism. However, because they are classified by drug registration bodies as nutritional supplements, they are not subjected to the same degree of rigorous testing and documentation as that required for registration of a pharmaceutical agent. It is therefore imperative to look carefully for objective evidence of a clinically-proven beneficial response to such products.

In Australia, a significant percentage of pet owners are also using one of the many health-food shop preparations marketed for relieving the symptoms of OA, sometimes for both themselves and their pets. Some of these are simple products with only one ingredient, whereas others are mixtures of a large number of compounds. There seem to be two concepts behind the “multiple-compound” nutraceuticals:

a) That synergism exists between the components resulting in an improved benefit to the patient over that achieved by the individual components.

b) Simple additive benefits from the different components, perhaps acting by different mechanisms (or influencing different pathways in the complex pathophysiology of OA).

Some products coming from New Zealand have incorporated green-lipped mussel extract with glucosamine and other cartilage matrix products, in the belief that both can play a role in managing the signs of OA. There is no doubt that with an ageing human population which includes a significant proportion of people attracted by the “natural therapy” concept, veterinarians must remain up with the play in this field so that we can objectively
advise clients of the best alternatives for treating OA in their pets. There have been a number of publications reporting the results of uncontrolled studies examining the benefits of green-lipped mussel extract on dogs with OA, but a recent placebo-controlled study showed more substantive evidence for its beneficial effects in dogs with clinical signs of OA (Pollard et al 2006).

The slow rate of change in symptoms raises another problem with assessing the efficacy of these compounds – OA is a chronic progressive disease with a clinical course, which is marked by waxing and waning of clinical signs, so it is difficult to separate a true beneficial effect from a change in the natural course of the disease. There is significant interest in the medical field over a very large multicentre clinical trial conducted in North America lasting a number of years and involving a very large number of patients. This study compared an NSAID with glucosamine alone, chondroitin sulfate alone, and a glucosamine/chondroitin sulfate combination in patients with knee OA. Only patients with moderate to severe knee OA and treated with the combination of glucosamine and chondroitin sulfate showed a significant improvement in clinical knee joint function when compared to placebo (NIH-funded study: Arth Rheum 52:9(suppl), p622, 2005)

Special diets for arthritic patients - a number of prescription diets for arthritic dogs (and more recently cats) have arrived on the market in Australia and New Zealand. There are two significant types of ingredients in these diets:

- glucosamine and chondroitin sulfate, which act the same way as orally dispensed nutraceuticals
- n-3 polyunsaturated fatty acids, which alter the substrates for the arachidonic acid inflammatory cascade, resulting in a shift towards the production of “less-inflammatory cytokines,” and consequently a reduction in synovitis in arthritic joints (Curtis et al 2002).

In my opinion, these diets should become an integral part of the management of OA in canine patients.

4. Corticosteroids:
Corticosteroids tend not to be commonly used in pet practice although they are favored by some greyhound practitioners to help extend the racing life of a dog. The disadvantages of intra-articular steroid therapy include osteoporosis of the underlying bone, risk of septic arthritis, morbidity of injection, and exacerbation of cartilage lesions associated with OCD and in cases of joint instability.

Other pain management strategies
Multimodal pain management strategies are widely used in human patients with chronic pain, and the application of some of these modalities to the management of canine and feline OA patients is increasing. The most common of these are neurotransmitter modulation (drugs such as gabapentin), acupuncture, and opioids (including transdermal patches and drugs such as tramadol).

Physical therapy – its role in the management of OA
Physical therapy is a very significant part of the management of OA in humans. Veterinarians have probably neglected this aspect of the management of joint diseases in our animal patients, justifying this neglect by
claiming poor patient and owner cooperation. While there is some validity in this excuse, many arthritic patients can be greatly helped by dietary management, weight loss, controlled exercise, heat/cold and massage therapy and passive joint manipulation. In addition, specific strengthening activities/exercises can be very beneficial to some arthritic patients. These aspects of patient management should be discussed with every client with encouragement to use these modalities in addition to the medical and surgical methods for managing OA.

The increasing recognition of the importance of physical therapy in the management of OA in dogs is beginning to appear in the literature in the form of clinical studies. A comparison of the post-operative function of dogs following cruciate repair with and without post-operative rehabilitation has been published. Using force-plate analysis of gait, the group that received rehabilitation were shown to be weight-bearing equally on both hind limbs 6 months post surgery whereas the dogs in the group managed by rest and exercise-restriction still showed reduced limb-function in the operated leg (Marsolais et al. 2002).

Summary and key points - treatment of osteoarthritis:

1. The primary aim is to restore as much pain-free function as possible to the affected limb.

2. OA is a chronic progressive disease with a complex set of inter-related disease pathways that leads to joint dysfunction. A multimodal approach offers the best chance of successfully controlling the symptoms of OA and thereby maintain quality of life.

3. NSAID therapy can provide effective control of joint pain and newer medications are associated with less side-effects. Individual dogs respond differently to different NSAIDs so a number of products should be trialled in non-responding cases.

4. Patients suffering lameness and locomotor dysfunction associated with chronic pain that is poorly responsive to NSAID therapy can benefit from additional pain management strategies including acupuncture, physical therapies, opioids and neurotransmitter modulating therapies.

5. Despite little sound evidence to support the benefits of their use, nutraceuticals are likely to remain very popular with a large section of the population of pet owners and veterinarians, particularly those who have experienced benefits from their use for their own arthritic problems.

6. Prescription diets including those for weight reduction and those with additives such as glucosamine and n-3 PUFA's can play a significant role in the overall management of joint disease.

7. Intra-articular corticosteroid therapy is a viable treatment for end-stage joint disease in cases where surgery is not planned, but is associated with significant patient morbidity of intra-articular injection.

8. Other causes of limb dysfunction apart from joint pain (eg proprioceptive abnormalities and myofascial pain) need to be explored in cases that fail to respond to medical therapy.

9. Physical therapy should be encouraged as an adjunct to medical and surgical therapies. Physical therapy
has a particularly important role to play in the perioperative period to assist rehabilitation following joint surgery.

10. OA is a progressive degenerative disease for which the treatment goal should be control of symptoms to maximise quality of life.

Conclusion

So…..does any treatment for OA really work? The answer is clearly yes, as long as the goal is control of symptoms. Clinicians must recognize the significant variation between individual OA patients in their response to various treatment types, and that multimodal therapy offers the best chance of maintaining pain-free mobility and therefore quality of life.

References