ASSESSING AND MANAGING CHRONIC PAIN IN CATS

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Abstract

There are numerous causes of long-term pain in cats including but not limited to neoplasia, dental and oral disease, inflammatory bowel disease, persistent post-surgical pain and non-healing wounds. However, osteoarthritis (OA) is the number one cause of long-term pain and suffering in cats. Associated behavioral changes with OA are subtle and often missed and because owners think this is normal "old-age" cats go untreated. Diagnosis and treatment are a team effort involving the owner, the veterinarian and other members of the clinic team. There are some validated assessment tools available which are valuable for both diagnosis and monitoring the efficacy of treatment. A successful approach to treatment is multimodal, using a combination of pharmacologic and non-pharmacologic approaches.

Keywords: osteoarthritis, feline, maladaptive pain, assessment, NSAID, non-pharmacologic

Introduction

Chronic pain has been defined in different ways. It can be linked to time, e.g. "any pain that lasts more than 3-6 months", but this set timeline may not be relevant in veterinary species with different life expectancies. Pain that "persists beyond the normal tissue healing time" is another definition. This latter definition suggests there is a demarcation between acute and chronic pain but in they may exist on a continuum.[1] It is important to understand that chronic pain is "without apparent biological value" but is the cause of suffering in animals and humans.

Based on the concept of successful treatment being based on treating the underlying cause, Woolf proposed that the two terms, *adaptive* and *maladaptive* be used to describe pain.[1]

Adaptive pain

Adaptive pain includes nociceptive and inflammatory pain. Nociceptive pain is activated by high threshold noxious stimuli (e.g. heat) and is a protective mechanism; it may or may not result in tissue damage but is essential for survival. Tissue damage (e.g. a surgical incision) results in inflammatory pain with local tissue becoming more sensitive to stimuli. Inflammatory pain is considered adaptive because it serves a purpose by helping the animal protect itself against further injury. It is usually easy to identify the cause and normally it is easy to treat, reversible or self-limiting.

Maladaptive pain

Maladaptive pain is not protective, it has no biological value, and should be considered a disease rather than a symptom. It results from changes in pain processing systems and is of two types:

1. *Neuropathic pain*; this is a result of obvious neural tissue damage (central or peripheral; it is important to acknowledge that one cause is surgical trauma).
2. *Functional pain*; no neural damage or inflammation is present, but the driving force for pain is a malfunction or dysfunction in the nociceptive system.

In maladaptive pain there is amplification and facilitation of "pain traffic" and increased sensitivity to stimuli. Pain can be spontaneous due to generation of nociceptive input from the central nervous system itself. Other things that contribute to maladaptive pain are an imbalance between inhibitory and excitatory nociceptive input, altered descending inhibition and decreased activation of endogenous analgesic systems and spontaneous ectopic discharge from injured nerves. Another term that is important to the concept of maladaptive pain is *central plasticity*

which is initiated through cellular wind-up. *Wind-up* is defined as a neuron's increased response and output following identical, repeated stimuli. The term central plasticity refers to an autonomous global response that continues after the stimulus stops, or which is sustained by low level nociceptor input in the periphery.[2] Because some processing systems are down-regulated the term central plasticity is more descriptive than central sensitization. These changes result in hyperalgesia or allodynia and expansion of the receptive field of neurons.(3)[3]

Examples of maladaptive pain

An obvious example of neuropathic pain is a nerve sheath tumor. Surgery causes nerve damage and if healing is abnormal, or acute pain management is inadequate this may lead to persistent postsurgical pain, a long-term and maladaptive condition; this is seen in some cats after onychectomy. Although the term is new to veterinary medicine cats with orofacial pain syndrome may have functional pain. In many long-term painful conditions in cats, there is a complex combination and overlap of adaptive and maladaptive pain. It is likely that with each disease and even in each individual, different neurobiological processes will be at play and vary over time, making treatment challenging and the response to analgesics unpredictable. The list of conditions with a pain component known to affect the wellbeing of cats over long periods is extensive and includes, but is not limited to, neoplasia, osteoarthritis, dental and oral disease, inflammatory bowel disease, persistent post-surgical pain and non-healing wounds.

Assessment tools

Owner evaluations are very important in the assessment of long-term pain because owners know their cat best and can assess behaviors that cannot be observed during a clinic visit (e.g. using a litter box, interaction with other people and pets in the household). There is a growing understanding of behaviors that may be related to musculoskeletal disease in cats, but one

assessment tool may not be applicable to all cats due to different lifestyles. The pain scales for cats with OA include the Feline Musculoskeletal Pain Index (FMPI)[4], the Client Specific Outcomes Measure (CSOM)[5], the Montreal Instrument for Cat Arthritis Testing (MI-CAT)[6] and the Owner Behaviour Watch (OBW).[7] (See resources for information on how to easily locate these tools). The FMPI and CSOM are questionnaire based and completed by the owner. The OBW asks owners to assess their cat within 4 major domains: general activity, mobility, temperament and grooming.[7] The MI-CAT is designed for veterinarians. A new series of videos have recently been developed to help veterinarians perform a systematic and useful feline orthopedic examination (www.zoetisus.com/oa-pain/feline-exam-videos.aspx). It is also helpful to ask owners to capture video clips of their cats in their own home environment. Objective measures of movement can be captured using activity monitors attached to cat's collars or harnesses. These accelerometers can separate cats with OA from normal cats.[8]

Quantitative Sensory Testing (QST)

QST measures the frequency or intensity of different stimuli required to elicit a patient response. The stimuli used include mechanical, heat, cold and vibration. When central plasticity is present changes in sensation to these stimuli occurs. QST is in its infancy in veterinary medicine, however by using mechanical sub-threshold repetitive stimuli, Guillot and colleagues could discriminate cats with osteoarthritis from non-affected cats.[9]

Quality of Life Scores

It was assumed that cats with OA would have a diminished QoL and this would be primarily linked to mobility impairment; however owners ranked 60% of things their cat did as "inactive" activities.[10] A large percentage of cats with OA also have chronic kidney disease or other comorbidities therefore an overall health related QoL (HRQoL) may be more valuable.[11] Two

are currently available: the CHEW questionnaire which still requires testing as a screening tool.[12] The other is an on-line tool (www.newmetrica.com).

Management of maladaptive pain

Maladaptive pain is complex, exists in a continuum and is seldom static. A combination of inflammatory and maladaptive pain is often present. Clear communication with the client is essential at the outset of a treatment plan. The owner must understand that comfort but not cure is the goal and that it is rare to achieve complete resolution of clinical signs. The financial and emotional cost, and time investment required should not be under-estimated. QoL assessments over time are essential as is a discussion of euthanasia as the treatment option when suffering can no longer be relieved. These discussions should start early and be revisited during treatment.

Approach to Treatment

Often the first treatment plan is a "best guess". A short analgesic trial can be used to gauge the response to a specific drug before long-term planning. This "trial and error" approach is what leads to disappointment and frustration, as the first plan does not always reap the desired results. A multimodal or integrative approach is required. The following owner and cat factors must be considered: drug burden (how many drugs and how often?), ease of administration (palatability, owner's skill), the cat's tolerance to drugs and their administration. Drug, and caregiver aversion is a possible outcome of drug treatment.

Pharmacologic Therapy - Primary Analgesics

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the primary class of drug used to manage OA in all species. We have less experience and fewer choices with chronic use of NSAIDs in cats than we do in other companion animals. Meloxicam has efficacy in cats with OA based on different methods of evaluation.[4, 7, 13] Many older cats with OA also have chronic kidney disease,

however studies show that, with caution, these cats can still benefit from NSAIDs. For a concise discussion of this topic see Monteiro and others 2019.[14] In a euvolemic state, renal perfusion is not prostaglandin (PG) dependent but in the face of hypovolemia or hypotension, vasodilatory PGs are important for maintaining perfusion. The owner and veterinarian should work together to find the lowest effective dose for each individual patient; in countries where it is authorized, the label dose of meloxicam is 0.05 mg/kg orally, once daily but many cats do well on doses of 0.01-0.03 mg/kg.[15] Robenacoxib has been studied in cats with OA, with and without kidney disease, over a 28-day period with no reported adverse effects.[16] This drug has recently received authorization for "treatment of pain and inflammation associated with chronic musculoskeletal disorders" in cats by the European Medicines Agency.

Other Analgesic Drugs

Tramadol has undergone pharmacokinetic and efficacy studies in laboratory cats and client owned cats. Although deemed efficacious in these studies, palatability and adverse side effects including, sedation, dysphoria, diarrhea and inappetence is a major drawback for clinical use.[17] Gabapentin is frequently prescribed by veterinarians, yet the efficacy of gabapentin has only recently been reported in a small group of cats.[18,19] Treatment was associated with improvement in activities that owners had identified as being impaired, but based on activity monitors overall activity levels were lower during treatment compared to a period of placebo treatment. Sedation was the most common side effect.[19]

Non-pharmacologic Treatments

Some of the commercially available "joint diets" that contain the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), green-lipped mussel extract and glucosamine/chondroitin sulfate are beneficial.[20] Physical rehabilitation modalities include but

are not limited to laser therapy, electrical stimulation, passive range of motion exercises, massage, trigger point therapy and therapeutic exercise. Acupuncture is also an option and many cats are very tolerant of this modality. Although there is a need for well controlled clinical studies using these techniques there is general agreement that many cats greatly benefit from these therapies. Many owners want to be part of the treatment plan for their cat and we can teach them how to perform some therapies. Cats with impaired movement need assistance with some "every day" activities. These include but are not limited to:

- Accessing elevated places – use steps, chairs and boxes to make this easier
- Eating and drinking – elevate food and water bowls
- Using a litter-box – ensure this is "easy entry" with a low access point
- Doing their "favorite thing" – this will be different for each cat
- Grooming – owners can assist with this

Emerging modalities for maladaptive pain

There has been a huge growth in the use of monoclonal antibodies to treat numerous diseases in humans and this has spilled over into veterinary medicine. Neutralizing antibodies to nerve growth factor (NGF) provide pain relief in humans, rodent models, dogs and cats with osteoarthritis.[21] A new class of drugs called the piprants are now available for the treatment of osteoarthritis associated pain in dogs. Grapiprant is a selective antagonist of the EP4 receptor, one of the four prostaglandin E_2 (PGE_2) receptor subtypes. There are likely to be fewer unwanted side-effects with this class of drug because the COX-1 and COX-2 pathways are not affected and the safety data in cats including when given at high doses encouraging.[22]

Maladaptive pain is common on cats, but progress has been made in understanding its etiology, raising awareness and developing new targeted therapies and treatment modalities.

Resources

Assessment tools: www.wsava.org/Committees/Global-Pain-Council.

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