Chronic Pain Management in Cats
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Chronic pain is maladaptive and is a significant clinical problem in cats. Properly assessing and managing chronic painful conditions such as feline osteoarthritis (OA), cancer and feline oral pain syndrome (FOPS) continues to be challenging (1-4). Feline OA is a significant clinical problem, particularly in older cats, as it can be associated with pain and mobility impairment (3, 5-7). Osteoarthritis involves a complex pain state with nociceptive, inflammatory and neuropathic components (8, 9). Facilitation of nociceptive temporal summation (7) and punctate tactile hypersensitivity (10) have been identified in cats with OA, suggesting the presence of central sensitization. An imaging study (11) revealed significant changes in the secondary somatosensory cortex, thalamus and periaqueductal gray in cats with OA compared to healthy controls, suggesting that the condition is accompanied by sustained nociceptive inputs and increased activity of descending inhibitory pathways. In humans, chronic pain alters the flow and integration of information across brain regions, effectively impacting brain function and behavior (12).

At present there is no gold-standard assessment tools for evaluating chronic pain and response to analgesics in cats. Changes in mobility assessed subjectively with client-specific outcome measures (CSOM) questionnaires, or objectively via accelerometers have been used for this purpose (10, 13, 14). But the ability of the CSOM to identify treatment effect with meloxicam compared to placebo has not been very consistent (13, 15). The CSOM enabled detection of significant changes after discontinuing treatment, as compared to placebo, presumably because of recurrence of clinical signs, but did not reveal changes during the treatment phase (15). The feasibility of using this approach in clinical practice has not been investigated, but the ethics of withdrawing analgesic treatment for the purpose of assessing pain relief should be considered. Objective evaluation of mobility with accelerometers correlate well with distance moved (16) and has more consistently detected treatment effects in activity levels (10, 13, 14). Other objective modalities include ground reaction forces (10) mechanical paw withdrawal thresholds (10), positron emission tomography (11) and goniometry (17) but some of them may not be easily applicable to everyday practice. An attempt to construct an arthritis-testing instrument for use by veterinarians in a colony of laboratory cats with OA was not successful (18). There continues to be a need to develop sensitive, valid and practical tools to assess chronic pain in feline patients.

Of the pharmacologic options to manage OA pain in cats, cyclooxygenase (COX) inhibitors were shown to alleviate pain and enhance mobility in cats with OA (13, 19, 20), although the central sensitization component may not be responsive to these drugs (10, 14). An important limiting factor in the United States is that COX inhibitors are not approved for long-term use in cats. These drugs can cause serious, life-threatening adverse effects (20-22). The company distributing meloxicam, the drug examined in one study (19), has issued a strong warning that it should not be used repeatedly in cats due to a high incidence of renal failure. These issues are even more concerning in geriatric cats, the population most likely to develop OA, because many have co-morbidities (23). While legitimate, these concerns limit or fully prevent the use of effective analgesics in many cats with OA-associated pain, as well as other painful conditions.

Multimodal therapy with tramadol and meloxicam, which is expected to simultaneously modulate ascending nociceptive input and descending inhibition, significantly decreased central hypersensitivity in cats with OA as assessed via mechanical temporal summation of pain (14). Tramadol has multiple mechanisms of action (24-27) and can be effective in the management of painful OA in humans (28, 29). Despite being commonly prescribed for chronic pain in cats and dogs, there is no published literature evaluating the use of tramadol as a single drug for this purpose in either species (30). Our recent observations suggest that oral tramadol (2 mg/kg twice daily) may be an option for pain management in geriatric cats with OA, although risk of central nervous system and gastrointestinal adverse effects exist (Manuscript accepted, JAVMA). Cat refusal to take oral tramadol that was prepared as a powder in gelatin capsules was an important challenge encountered in that study. Tramadol reportedly has a bitter taste, which appears to be unpleasant to cats. Interestingly, chronic pain in people is associated with a significant increase in sensitivity to taste. It appears that taste is co-localized with pain in the central nervous system. The gustatory stimuli becomes more intense but not more or less pleasant/unpleasant (31). If also true in cats, this could make it more difficult to administer medications with unpleasant taste, as cats would presumably be able to detect the substance at a much lower threshold.

Gabapentin, a structural analogue of γ-aminobutyric acid (GABA) originally developed as an antiepileptic drug, was found to be effective in the treatment neuropathic pain states in people (32, 33). It resembles GABA however it does not act at GABA receptors and instead it selectively inhibits voltage-gated calcium channels containing the α2δ–1 subunit (33). Gabapentin decreases nociceptive input via suppression of dorsal horn nociceptive neurons (34) and stimulate descending inhibition via increasing glutamatergic neurotransmission in the locus coeruleus (35). In cats, gabapentin is characterized by a small volume of distribution and low clearance (36). It does not reduce inhalation anesthetic requirement nor increase thermal nociceptive thresholds in healthy cats (37, 38) but analgesic benefits were reported in two cats with multiple injuries (39). In cats, gabapentin is frequently recommended for the management of chronic pain,
including pain associated with OA (3, 40) but the strength of the evidence is low as there are no controlled studies (41). In cats with FOPS, which presumably is associated with neuropathic pain, gabapentin appears useful for managing their pain (1). Our studies in geriatric cats with OA indicate that oral gabapentin (10 mg/kg twice/day) significantly decrease accelerometer-based activity level, presumably because of sedation, but improved owner-identified impaired activities as well as owner-perceived quality of life (Manuscript accepted, JAVMA).

Amantadine, originally used in humans to treat influenza, has also been shown to be an antagonist of N-methyl-D-aspartate (NMDA) receptors (42). NMDA receptor activity plays a central role in the etiology of central sensitization and chronic pain (43), processes that are present in cats with OA (7, 11). The pharmacokinetics of amantadine in cats have been published (44). Although efficacy data are lacking, amantadine has been indicated as analgesic option for chronic pain cats (3, 41). Mechanistically, amantadine may be a useful analgesic in feline OA, but this hypothesis requires formal investigation before its clinical use can be recommended.

Nutrition may be particularly important in relieving pain, especially in OA. A diet rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and supplemented with glucosamine/chondroitin improved mobility in cats with OA (45). Complementary therapies and rehabilitation medicine are increasingly being introduced in the treatment of chronic painful conditions in small animals, especially dogs but also in cats (2, 4). Anecdotal accounts in veterinary patients indicate that these can be very effective in improving measures of pain and quality of life. However, studies are needed to definitively assert the efficacy of these modalities.

References:

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