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EDITORIAL

Nonsteroidal anti-inflammatory drugs in the cat

The recognition of pain in the cat is difficult when compared to other species of domestic animals and humans. Acute pain is probably easier to recognise than chronic pain in the cat. Animals in acute pain will often remain quiet and immobile and have a tense appearance. Occasionally they may become aggressive and resent handling. Vocalisation is relatively rare apart from the occasional growl although this may to some extent be related to the breed of cat. In fact, they may even continue to purr. During recovery from major surgery cats may demonstrate a manic reaction on emergence from anaesthesia which may be difficult to differentiate from an acute pain response. If acute limb pain is severe they may attack a dressing or even attempt to discard it. This behaviour may be accompanied by considerable vocalisation. After abdominal surgery, cats which are in pain may adopt sternal recumbent position and tense their abdominal muscles. If post-operative pain is present in the facial region cats may attempt to rub or scratch the affected area which may compromise a successful outcome to the procedure (Flecknell and Waterman-Pearson 2000). Chronic pain is often associated with a number of conditions including neoplasia, oral disease, wounds and dermatitis in addition to osteoarthritis and degenerative joint disease. The incidence of these latter conditions has probably been underestimated in cats (Clarke et al. 2005). The behavioural changes associated with these conditions may be insidious in onset and easily missed and are often attributed by the owner to the 'ageing process'. Lameness or exercise intolerance are not common complaints by owners. There may well be behavioural changes which can generally be classified as a reduced ability to 'care for themselves' and an inability or reluctance to jump, particularly up onto or down from surfaces. It may well be that these changes are so subtle that they are not appreciated by owners until they observe the obvious improvement after appropriate analgesic therapy (Robertson 2006).

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) in cats is the subject of a review in this issue of the journal (Lascelles et al. 2007). These drugs are a group of weak organic acids, carboxylic acids (aspirin, carprofen) and enolic acids (meloxicam, phenylbutazone). Their main therapeutic effects of reduction of fever, pain and inflammation are due to their inhibition of prostaglandin production from arachidonic acid by the cyclooxygenase (COX) enzymes. There are two distinct forms - COX-1 and COX-2. COX-1 is involved in the regulation of gastrointestinal and renal blood flow and has a role in blood clotting. In contrast, COX-2 is an inducible enzyme which is expressed at the sites of inflammation in response to inflammatory mediators. Earlier published work had indicated that the prostaglandins that mediate inflammation were produced by COX-2 whereas those that were important in gastrointestinal and renal function were produced via COX-1. This gave rise to the belief that NSAIDs exerted their useful therapeutic effects by COX-2 inhibition, whilst the inhibition of COX-1 was considered to be responsible for some of the toxic side-effects. It is now clear that this was very much an oversimplification and that the whole subject is more complex and species differences may also be important. Most NSAIDs are metabolised in the liver and excreted via the bile duct or kidneys. As the cat has a reduced ability for glucuronidation of drugs then it follows that agents (aspirin, carprofen) which are metabolised by this route will have a longer drug elimination half-life in this species than in the dog. In contrast, drugs (meloxicam) which are cleared by oxidative enzymes have a similar or reduced half-life in cats when compared to dogs. A number of adverse effects, following the administration of NSAIDs have been reported in cats. However, renal effects appear to be relatively rare following a single dose of carprofen or meloxicam to healthy cats. It is under conditions of dehydration, hypovolaemia and hypotension, that NSAIDs may

impair auto regulation and lead to produce a decrease in renal blood flow often progressing to acute renal failure and death. Whilst gastrointestinal ulceration is known to occur in a number of species following NSAID administration, the situation in the cat appears to be far from clear as to the mechanisms involved. It is well known that NSAIDs affect haemostasis by their effects on platelets and vascular epithelium. Aspirin has been used as an anticoagulant in the cat and other agents have been studied for their effects on clotting in relation to surgery and the situation is again far from clear. However, none of the NSAIDs which have licence/approval have been evaluated for their effects on clotting and no significant changes have been reported. If cats should accidentally ingest NSAIDs then an emetic should be administered within the first hour and after that activated charcoal has been recommended. Treatment is basically on a symptomatic basis with the administration of fluids and supportive therapy with H_2-receptor agonists or protein pump inhibitors to reduce the gastrointestinal effects.

Carprofen has been licensed/approved for use in a number of countries. Its use is recommended for the control of perioperative pain as a single dose of 4 mg kg^{-1} administered subcutaneously (SC) or intravenously (IV). It is not recommended for repeated use due to a wide variation in inter-cat pharmacokinetics. Flunixin is not licensed or approved for use in the cat. However, it has been used off-label at a dose of 0.5–1 mg kg^{-1} administered either IV or orally (PO). Ketoprofen is licensed/approved for use in cats in a number of countries and there are a number of published reports on its use. It is generally administered PO at a dose of 2 mg kg^{-1} followed by 1 mg kg^{-1}. A maximum of five days usage is recommended. In the treatment of chronic pain a dose of 1 mg kg^{-1} PO for five days produced a clinical improvement.

Meloxicam has been licensed/approved for use in the cat in a number of countries. It is recommended for use in perioperative analgesia at a dose of 0.3 mg kg^{-1} SC. If additional analgesia is required then off-label doses can be administered for 2–3 days at a dose of 0.025–0.5 mg kg^{-1} PO. A number of reports have been published on its off-label use in cats for the treatment of chronic pain. An initial dose of 0.1 mg kg^{-1} either SC or PO followed by 0.05 mg kg^{-1} for 1–4 days and then reduced to the lowest effective dose of 0.025 mg kg^{-1} administered every 24–48 hours. The animals must be monitored closely for any side-effects. Other workers have recommended a dose of 0.1 mg kg^{-1} PO 2–3 times a week. More recently, however, a licence has been granted for the use of meloxicam in a special oral suspension preparation for cats. It is less concentrated (0.5 mg/ml) than that used in dogs which facilitates more accurate dosing in smaller patients. It should not be used after SC dosing of meloxicam or any other NSAID or corticosteroid. A dose of 0.1 mg kg^{-1} PO should be administered on the first day followed by a daily maintenance dose of 0.05 mg kg^{-1}. Currently it is not recommended for use following injection as appropriate dosage regimes have not been established. Tolfenamic acid is licensed/approved for use in cats, for the treatment of febrile conditions and upper respiratory tract infections, in a number of countries. A daily dose of 4 mg kg^{-1}either SC or PO is recommended for 3–5 days usage although it has been suggested that it should not be used for more than two days.

The proper use of NSAIDs involves the use of the products within the indications for which they are licensed but the conditions of a licence may vary between different countries. If the drugs are administered off-label then this should be discussed with the owner and specific consent sought and obtained. Special attention must be paid to the development of clinical signs of toxicity and rapid and appropriate action taken. For acute and perioperative pain both carprofen and meloxicam are licensed for use in cats but should be avoided in the presence of dehydration, hypovolaemia and hypotension. As ketoprofen affects platelet activity its use should be limited to the postoperative period. No NSAIDs should be administered together or with corticosteroids and fluid therapy is strongly recommended when these drugs are used preoperatively in cats. If there are any suggestions of impaired organ function then appropriate laboratory tests should be performed before the administration of NSAIDs. Repeated administration of the drugs off-label is to be discouraged particularly in view of the recent licensing of meloxicam for cats. However, if they are used off-label then the lowest dose to have a therapeutic effect should be selected and routine laboratory tests for organ function should be carried out on a regular basis.

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