ANALGESIA – NSAIDS AND THEIR ROLE IN ORTHOPAEDIC SURGERY

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Gareth Richardson examines the importance of pain relief during orthopaedic procedures and advocates a multimodal and balanced approach to analgesia

IT IS important to control and alleviate pain after surgical procedures for the welfare of the patient, for ethical reasons, to help decrease the risk of complications, as well as to facilitate the healing process and avoid the development of chronic pain or wound interference (Lafuente et al, 2005; Deneuche et al, 2004).

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” (Horstman et al, 2004). Most veterinary surgeons accept that animals feel pain, but have difficulty in assessing the degree of pain felt after surgical procedures due to the absence of verbal communication between veterinary surgeon and patient (Horstman et al, 2004).

Orthopaedic surgical procedures involve considerable pain. Fracture repair is considered one of the most painful procedures in human medicine and is considered to cause moderate to severe pain in veterinary patients. Provision of adequate analgesia in patients undergoing fracture repair is essential, but remains a challenge (Bergmann et al, 2007).

Unfortunately, cats often receive analgesic medications for postoperative pain relief less frequently than dogs, mainly due to concerns about possible adverse effects (Romans et al, 2005). The quantitative measurement of clinical pain in animals is difficult because it is a personal experience

that is unique to every individual (Deneuche et al, 2004), so it is not surprising that the measurement of pain for clinical or study purposes has been the subject of much debate. In order to assess the efficacy of analgesic drugs under clinical conditions, different pain scoring systems have been advocated to try to assess postoperative pain objectively in dogs. These include the visual analogue scale, behaviour (such as vocalising), and physiological markers of pain, such as plasma catecholamine or cortisol levels (Horstman et al, 2004).

This difficulty in recognising clinical pain has led to analgesic drugs being underutilised in veterinary surgery. A study in France revealed that 16.3 per cent of French practitioners do not use any analgesics for potentially painful orthopaedic procedures (Deneuche et al, 2004), while similar studies in other countries have shown that only 48 per cent of practitioners used analgesia in similar circumstances (Dohoo et al, 1996; Capner et al, 1999).

These studies suggest various reasons for vets withholding analgesia, including an inability to recognise pain, fear of adverse reactions or toxicity associated with analgesic use, fear of theft and misuse of opioid drugs within the practice setting, as well as the legal administration and record keeping surrounding opioid use (Deneuche et al, 2004). The author has witnessed all of these reasons given to justify not giving analgesia in private practices in which he has worked in the UK.

Adverse effects

Traditionally, the most widely used analgesic drugs after orthopaedic procedures have been opioid drugs. These are effective analgesics, but may be accompanied by sedation, dysphoria and respiratory and cardiovascular depression, especially at high doses (Deneuche et al, 2004).

Considering these adverse effects and the potential for theft and personal abuse within a practice setting, an alternative to opioid analgesia is desirable from a medical and an administrative aspect (Deneuche et al, 2004).

NSAIDs have been found to provide analgesic effects similar to injectable opioids (Mollenhoff, 2005; Lafuente, 2005), with carprofen providing very effective analgesia (Nolan et al, 1993; Lascelles et al, 1994; Grisneaux et al, 1999). It is generally accepted that the pre-emptive administration of a combination of analgesic drugs, commonly the administration of opioids and NSAIDs, is an effective way of reducing the severity and duration of postoperative pain (Grisneaux et al, 1999). The action of NSAIDs includes peripheral and central effects. The peripheral effect is due to inhibition of the cyclooxygenase (COX) enzyme. This enzyme participates in the synthesis of inflammatory mediators, such as prostaglandins and thromboxanes. Cyclooxygenase occurs in two isoenzymes – COX-1 and COX-2.

The mechanism of activation and the final actions of these isoenzymes differ. COX-1 is capable of expression in most tissues and is especially relevant in gastric mucosa and kidneys where its expression results in protective effects. COX-2 expression results in release of inflammatory

mediators, such as prostaglandin, leading to inflammation of the tissue (Lafuente et al, 2005). The reduction of induced prostanoids inhibits cytoprotective functions on the gastric mucosa, affects primary plug formation of platelets, and modulation of vascular tone of the kidney (Deneuche et al, 2004).

The central effect is attributed to inhibition of COX-2 at the spinal and supraspinal levels. In response to nerve injury this enzyme is upregulated in the spinal cord and brain, leading to increased spinal prostaglandin E2 synthesis and cerebrospinal fluid (CSF) concentrations, and then to central sensitisation and hypersensitivity. Systemic administration of NSAIDs is thought to result in CSF and cerebrospinal concentrations sufficient to inhibit COX-2 and thereby prevent prostaglandin E2 synthesis and reduce the pain response (Lafuente et al, 2005).

NSAID administration for postoperative analgesia in dogs may be associated with side effects on renal function, on the gastrointestinal tract, and on coagulation (Deneuche et al, 2004). Among the adverse reactions caused by NSAIDs, gastrointestinal problems are the most frequent, regardless of the route of administration. In animals, gastrointestinal effects range from mild gastritis and vomiting to severe gastrointestinal ulceration, diarrhoea, bleeding, and even death.

Reported cases of renal toxicity occurred when high doses of NSAIDs were used or when there were other complicating factors, such as impaired renal perfusion caused by dehydration, anaesthesia, shock or preexisting renal disease. However, NSAID-induced renal insufficiency is usually temporary and reversible with drug withdrawal and administration of IV fluids (Deneuche et al, 2004). Because many adverse effects of NSAIDs are attributable to the inhibition of the normal physiological role of prostaglandins (COX-1 mediated), NSAIDs that are specifically inhibitory of COX-2, but not COX-1 (Lafuente et al, 2005) have been developed.

This type of COX-2 selective NSAID drug includes carprofen and meloxicam, and these drugs have generally superseded the use of ketoprofen – an NSAID that inhibits both COX-1 as well as COX-2 isoenzymes. Carprofen, a weak inhibitor of COX enzymes, has been found to provide good analgesia without side effects, when administered pre-operatively to dogs undergoing a variety of orthopaedic procedures (Nolan et al, 1993; Lascelles et al, 1994).

Evidence

Subjective pain scores in dogs after major orthopaedic surgery have been shown to be signifi– cantly lower in animals administered the injectable formulation of carprofen pre-operatively when compared to a placebo given at the same time. Carprofen has also been shown not to cause clinically relevant adverse effects in dogs where fractures have been repaired after five days of treatment, even when it was administered before surgery or given to patients with trauma-induced alterations in renal function or haemostasis (Bergmann et al, 2005). In addition, it has been found that carprofen and buprenorphine are well tolerated analgesics for a five-day administration in cats (Mollenhoff et al, 2005).

The subcutaneous (SC) administration of carprofen and meloxicam have also been shown to provide similar postoperative sedative and analgesic effects. Carprofen has been observed to provide effective analgesia for up to 20 hours after anaesthesia in dogs (Lascelles et al, 1994; Slingsby, 2001). It has also been reported that meloxicam can control postoperative pain for up to 20 hours in dogs undergoing abdominal surgery (Mathews et al, 2001). Both meloxicam and carprofen can be considered effective in controlling orthopaedic postoperative pain for up to 24 hours. NSAIDs can also help reduce swelling after orthopaedic surgery because of their antiinflammatory action (Deneuche et al, 2004).

Although there is evidence that NSAIDs inhibit bone formation, and therefore delay healing in orthopaedic procedures, the control of pain remains of paramount importance and there is insufficient evidence to recommend withholding their use. Fractures and osteotomies can heal in the presence of NSAID administration and NSAIDs are important for their potent anti-inflammatory and analgesic effects after bone injury.

However, when the speed and effectiveness of bone healing is of particular importance, such as in cases of delayed union, non-union, tenuous orthopaedic repairs or in patients where delayed bone healing is expected, it is prudent to consider the evidence when prescribing NSAIDs (Barry, 2010).

Higher doses and longer duration of treatment with NSAIDs appear to have a greater detrimental effect on bone healing, therefore it makes sense to discontinue NSAID treatment after a reasonable post-injury period if it is no longer needed for analgesia (Barry, 2010). It has also been shown that treatment with deracoxib postoperatively did not provide better clinical outcomes when dogs were subjected to intense rehabilitation after tibial plateau levelling osteotomy (Gordon-Evans et al, 2010).

Reports have shown that perioperative use of NSAIDs in conjunction with opioid analgesics have led to decreased human patient pain intensity levels, increased patient satisfaction, and, on average, 40 per cent less morphine use after major orthopaedic surgery. Therefore, the decreased amount of opioid analgesic needed will lead to less patient morbidity and greater client satisfaction. Although human reports support the use of NSAIDs after orthopaedic surgery, the results in the veterinary literature have been conflicting (Bergmann et al, 2007).

Finding the balance

Administration of one drug is often not sufficient for postoperative analgesia. Multimodal or balanced analgesia combines different analgesic techniques, such as epidural analgesia, and drugs, such as NSAIDs and opioids, to achieve beneficial additive or synergistic analgesic effects. This allows for lower doses of analgesics to be administered, which may potentially alleviate their side effects. NSAIDs administered as a single agent lack the potency required for adequate analgesia in the immediate postoperative period after orthopaedic procedures. When NSAIDs are used in combination with opioids or local anaesthetics they can provide an additive effect because

of their separate mechanism of action (Bergmann et al, 2007).

The author therefore considers the administration of NSAIDs, such as meloxicam or carprofen, together with parenteral, transdermal and/or epidural opioids, should be the treatment of choice to reduce, or even eliminate, the pain and stress suffered by dogs after orthopaedic procedures.

Protocol

In our practice we use multimodal and balanced analgesia, and the requirements are tailored to suit each individual patient depending on clinical condition, underlying medical issues, and the type of orthopaedic procedure that is to be performed.

A healthy dog with normal serum biochemistry and haematology parameters that is undergoing an elective orthopaedic procedure, such as a Zurich cementless total hip replacement (Figures 1 **and** 2), would routinely receive the following analgesic protocol: 0.02mg/kg acepromazine and 0.2mg/kg methadone given SC as a premedication. In addition, 4mg/kg carprofen is given SC at induction and a transdermal fentanyl skin patch of appropriate strength for the size of patient is applied to the skin at the base of the tail directly after induction. The carprofen would be repeated 24 hours after the initial dose and the fentanyl patch would be left in situ for 36 hours, covered with appropriate dressings.

This protocol is varied for other orthopaedic procedures, for example, a bupivacaine solution may be applied intra-articularly (Van Vynckt et al, 2010) in cases of anterior cruciate ligament surgery (taking care not to exceed a total dose of 1mg/ kg), or epidural analgesia may be used in cases of tibial osteotomy, such as a triple tibial osteotomy, severe pelvic fractures, or triple pelvic osteotomies. Bupivacaine may also be used as a regional block (1ml-2ml of a 0.5 per cent solution given perineurally), such as in cases requiring rib resection. An oral course of carprofen is usually prescribed at 2mg/kg every 24 hours for the first week postoperatively. These analgesic protocols are also modified depending on clinical parameters. For example, NSAIDs will not be used in cases of renal failure or severe hypovolaemia.

Similarly, an otherwise healthy cat undergoing an orthopaedic procedure would receive the following analgesic protocol: pre-medication with medetomidine 10µg/kg given SC together with either morphine sulphate at 0.1mg/kg or buprenorphine at 20µg/kg, depending on the procedure to be performed.

Meloxicam (0.3mg/kg) is given SC at induction. Transdermal fentanyl skin patches and bupivacaine local anaesthesia are used in a similar manner as described with dogs, if indicated. Analgesia is maintained by means of postoperative injections of buprenorphine if that was the agent used in the pre-medication protocol, or with transdermal fentanyl if morphine was the agent used in the pre-medication protocol. These protocols are also adapted to match the patient's clinical parameters and the type of orthopaedic surgery planned (Figures 3 **and** 4).

It is important to use multimodal and balanced analgesia in orthopaedic cases to maximise patient comfort and optimise clinical outcomes. It is good practice to develop and individually prescribe a pain regimen for each patient, taking into account the medical condition and type of surgery to be performed, rather than adopting a blanket approach to analgesia. NSAIDs play a very important role in analgesic plans and will continue to do so.

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