Anesthetics & Sedatives, examines the use of RIMADYL (NSAID) approved by the Food and Drug Administration (FDA) for controlling postoperative pain in dogs which has more than 10 years of clinical studies.

In a new technical bulletin from Zoetis Inc, Sharon L. Campbell, DVM, MS, DACVIM, Medical Lead for Analgesics, Anesthetics & Sedatives, examines the use of RIMADYL Injectable to control postoperative pain for both soft tissue and orthopedic surgeries.

A Brief Discussion of Pain

Pain is an unpleasant sensory and emotional experience associated with tissue damage. The pain pathway has four distinct stages, starting with transduction and ending with perception (Figure 1). Along the pain pathway, the pain signal can be modified (either increased or decreased) by physiological or pathological changes or by pharmacological interventions.

Pain can be categorized as either: 1) physiological pain, also known as nociceptive pain; or 2) pathological pain, which includes: inflammatory pain (due to tissue damage); chronic pain, also referred to as maladaptive pain; and neuropathic pain (due to nerve damage).

Surgical pain is inflammatory pain and occurs after damaged cells release ions and inflammatory mediators, such as prostaglandins. This inflammatory response causes the peripheral pain neurons to become sensitized, a condition known as peripheral sensitization.6 The clinical result of peripheral sensitization is primary hyperalgesia, an exaggerated and prolonged response to pain stimuli (Figure 2).

The sensitized peripheral nerve fibers bombard the dorsal horn neurons with neurotransmitters, resulting in sensitization of these neurons, which is referred to as central sensitization (Figure 2). Central sensitization contributes to the exaggerated response to a pain stimulus through 1) secondary hyperalgesia, in which the area surrounding the site of injury becomes painful and 2) allodynia, in which the mere sense of touch can be perceived as painful. With appropriate pain management, both peripheral and central sensitization will resolve after the injury heals.6 However, when trauma is severe or when pain is not adequately treated, the patient could develop chronic pain. Successful management of surgical pain is required to prevent development of chronic pain.

Addressing Surgical Pain

Although general anesthetic drugs render a patient unconscious, these drugs do not interfere with the development of peripheral and central sensitization. RIMADYL inhibits cyclooxygenase-2 (COX-2) enzymes, therefore decreasing prostaglandin production at the surgical site and reducing peripheral sensitization. RIMADYL also inhibits COX-2 enzymes within the dorsal horn, therefore reducing central sensitization.6

Perception

After the primary sensory neurons synapse with dorsal horn neurons, the pain signal is projected to different areas within the brain, allowing the sensation of pain to be perceived. Opioids provide analgesia by decreasing the perception of pain.

NSAIDs and Opioids

For control of postoperative pain, experts recommend a multimodal approach which includes the use of analgesic drugs pre, intra, and postoperatively. Pain management should continue until the pain and inflammation have resolved to adequately address surgical pain, and prevent development of chronic pain. Since inflammatory mediators, including prostaglandins, play a critical role in the development of postoperative pain, NSAIDs are routinely used in both human and veterinary medicine to manage surgical pain.

NSAIDs and opioids are often used together to treat surgical pain. Opioids bind to opioid receptors in the dorsal horn and the central nervous system, resulting in analgesia. NSAIDs provide analgesia by decreasing inflammation at the site of injury and inhibit COX-2 enzymes within the dorsal horn. Because NSAIDs and opioids have different mechanisms for analgesia, they work together as part of a multimodal approach to pain management.

Ultimately, the final decision on which drugs or combination of drugs to use must be made on a case-by-case basis, taking into consideration the physiological status of the patient and the degree of pain associated with the surgery.

Dr Campbell also points out that maximizing the benefits and minimizing the risks of NSAIDs or any drugs used in an anesthesia and pain management protocol should involve appropriate patient selection, assessing the level of analgesia required, supporting the patient during surgery to maintain vital organ function, monitoring the patient’s response, and accordingly adjusting the patient’s environment.

FIGURE 1 The Classical Pain Pathway

**FIGURE 2 Surgical Inflammatory Pain, Peripheral and Central Sensitization**

Tissue damage that occurs after surgery results in a dramatic change of the chemical environment peripheral pain neurons, due to the influx of inflammatory cells (mast cells, macrophages, and lymphocytes) and releases a number of inflammatory mediators, including prostaglandins, referred to as the “sensitizing soup.”

The inflammatory mediators act directly on the peripheral pain neurons’ receptors (nociceptors), initiating a pain signal (transduction) and sensitizing the receptors, resulting in peripheral sensitization.

Changes associated with central sensitization lead to allodynia and secondary hyperalgesia.

A copy of the complete technical bulletin is available from Zoetis representatives or by calling 1-888-ZOETIS-1 (1-888-963-8471).

RIMADYL provides advantages over opioids

A single SC injection of RIMADYL, at 4.4 mg/kg (2.0 mg/lb), delivers effective pain relief for 24 hours. In contrast, most opioids are short-acting and necessitate multiple dosing and continuous i.m. infusion to deliver analgesia over a 24-hour period.

Due to its anti-inflammatory effects, RIMADYL injectable decreases swelling and controls pain at the surgical site sooner than opioids.

Because RIMADYL has both injectable and oral formulations, each providing 24 hours of analgesia, RIMADYL can be used both pre-surgery and can be administered at home by the owner to provide continuous analgesia.

This article concludes next month with a case study examining the benefits of using RIMADYL perioperatively in soft tissue surgery.

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6 Dose: See label. 8.4 mg/kg (3.8 mg/lb) may be used in cats >2 lbs and dogs >10 lbs. 5.6 mg/kg (2.5 mg/lb) is adequate for small dogs and cats. Efficacy of oral RIMADYL has not been established in small cats. 9.6 mg/kg (4.4 mg/lb) is recommended for all dogs greater than 20 lbs. 5.6 mg/kg (2.5 mg/lb) is adequate for small dogs and cats. 4.4 mg/kg (2.0 mg/lb) is recommended for all cats over 2 lbs.

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7 Due to the oral route of administration, RIMADYL can be administered preoperatively or postoperatively, for the prevention of pain in dogs undergoing surgical procedures requiring general anesthesia. 8.4 mg/kg (3.8 mg/lb) is adequate for small dogs and cats. Efficacy of oral RIMADYL has not been established in small cats.

8 The sensitized nociceptors increase the influx of inflammatory cells to the sensitized nerve to the dorsal horn of the spinal cord.