Case Study: Acute Visceral Pain in A Dog

Introduction

Control of pain from surgery and trauma is generally addressed in a patient's overall medical plan. However, pain from medical conditions is often overlooked or underestimated. In this case report of a dog with gastroenteritis, visceral pain is described and compared to somatic pain. Treatment of visceral pain and the use of the Composite Measures Pain Scale Short Form for identification of visceral pain are discussed.

Clinical Report

A 4-month-old 5.8-kg mixed-breed male intact dog was presented to the veterinary hospital with acute vomiting and diarrhea of or approximately 6-hours duration. The dog was obtunded, weak, estimated to be approximately 5% dehydrated, febrile (104.2F) and tachycardic (160 bpm). Abdominal palpation revealed a slightly distended abdomen and elicited whimpering and tensing of the muscles, both presumably due to abdominal pain. During the exam the dog voided hemorrhagic diarrhea. The caregiver reported that the dog had been lethargic and anorexic for approximately 24 hours and that there had been no abnormal ingestion of food, garbage, etc… prior to the anorexia. The dog had access to other dogs in its neighborhood and was unvaccinated. Other than hemoconcentration and low white blood cell count count, the serum chemistry and complete blood count were unremarkable, probably due to the fairly short time between onset of vomiting/diarrhea and admission to the hospital. Gastroenteritis (GE) caused by canine parvovirus type-2 (CPV) was diagnosed using a fecal enzyme-linked immunosorbent assay (ELISA) test. The dog was immediately hospitalized and placed in an isolation ward.

An IV catheter was aseptically placed in the right cephalic vein and administration of a balanced isotonic electrolyte crystalloid fluid (lactated Ringer's solution; LRS) was started at a rate of 75 mls/kg/24 hours. The dog was not hypoglycemic but the order was to recheck glucose in two hours and add dextrose to the LRS if necessary. Ampicillin (25 mg/kg) and maropitant (1 mg/kg slowly) were administered IV.

An hour after initiating therapy the dog was slightly more alert and less tachycardic (138bpm) but had started intermittently spontaneously vocalizing (whining) and reacted more vigorously to abdominal palpation, presumably due to increasing pain. The Glasgow Composite Measure Pain Scale-SF (CMPS-SF)[1] was used without section B (rises/walks) to score pain. This section was

omitted since the dog needed to stay in its cage to decrease environmental contamination with CPV. The initial score was A-I=1; A-II=0; C=5; D-V=4; D-VI=3 = Total 13, which is above the recommended treatment cut-off of 5 when not using section B.

When using the primary types of pain as nociceptive, inflammatory, neuropathic and functional,[2] the type of pain in this case was primarily inflammatory pain from viral damage to the cells in the mucosal layer of the intestinal lumen. The extensive damage caused to the mucosa likely initiated peripheral sensitization which commonly leads to central sensitization, thus hyperalgesia is often a component of visceral pain from mucosal damage.[3,4,5]

Buprenorphine (0.03 mg/kg) and a lidocaine bolus (1 mg/kg over several minutes) were administered IV followed by an IV lidocaine infusion (3 mg/kg/hour). One hour after initiating analgesia the dog was more active and alert, no longer whining and had reduced reactivity when the abdomen was palpated. The SFGCMPS score was A-I=0; A-II=0; C=2; D-V=1; D-VI=1 = Total 4. The SFGCMPS score continued to decrease, reaching 0 at 12 hours after initiating analgesia.

Buprenorphine was continued q6h for another 48 hours and then decreased to BID for the 24 hours prior to discharge. The lidocaine infusion was maintained at 3 mg/kg/hour for 24-hours at which time the lidocaine was decreased to 1.5 mg/kg/hour for another 24 hours and then discontinued. Maropitant was continued SID for 3 days total. Pain scoring was continued with decreasing frequency for the remainder of the dog's hospitalization. The only score during the final 24-hours in the hospital that was not a zero was on the final day of hospitalization when the dog received a 2 in D-IV because it was restless. Based on lack of response to abdominal palpation, this was deemed to be more likely due to the desire to leave a cramped cage than due

to pain. Other patient care (return to feeding, switch to oral fluid intake, etc…) was provided per the procedures used in our hospital.

Clinical Outcome

The dog made a full recovery and had a zero pain score at discharge which was approximately 72 hours after admission. No analgesic drugs were dispensed but the owners were instructed to monitor for signs of pain and to bring the dog back to the hospital if pain returned.

Discussion & Critique

Visceral pain is complex, not as well-understood as somatic pain and somewhat different from somatic pain.[3,4,5] Visceral nociceptors are the free nerve endings of A-delta and C fibers like somatic nociceptors and depolarize in response to inflammation, distension (stretch) and ischemia but generally not to mechanical stimuli unless inflammation is present. [3,4,5]

Unlike somatic pain, visceral pain is most often diffuse and difficult to localize.[3,4,5] This occurs because 1) visceral innervation is more sparse than somatic innervation, 2) nerves from the viscera tend to distribute over several spinal segments on entering the spinal cord and 3) visceral input often converges in the spinal cord with input from other structures, causing referred pain at sites potentially distant from the inciting pain. The viscera has a larger proportion of unmyelinated C-fibers so the pain is often described as dull, but can be sharp as occurred in our patient because A-delta fibers are also present.[3,4,5] Finally, visceral nerves often accompany

nerves from the autonomic nervous system and autonomic changes such as nausea, vomiting and vasomotor changes occur more commonly with visceral than somatic pain. [3,4,5]

The pain in this patient with gastroenteritis was primarily due to inflammation of the visceral mucosa from damage by the CPV along with stretched intestinal lumen from gas/diarrhea-induced distension. Because of the profound mucosal damage/inflammation that the virus causes, it is likely that peripheral and central sensitization also occurred, which might explain the fairly dramatic increase in the response to abdominal palpation between the first and second assessment.

Nociceptors are high threshold, meaning that only a painful - or noxious - stimulus should cause them to depolarize.[6] However, inflammatory mediators (prostaglandins, nerve growth factor, substance P, etc.) released from damaged tissue lower the depolarization threshold, or 'increase the sensitivity', of the nociceptor to noxious stimuli. This can cause the nociceptor to depolarize to a weakly painful stimulus or nonpainful stimulus and/or to depolarize spontaneously. This increased sensitivity is termed 'peripheral sensitization'. The increased number of action potentials occurring due to peripheral sensitization can lead to central sensitization, which is an amplification of the pain level that occurs in the in the spinal cord. The main mechanism of central sensitization is extrusion of the magnesium plug that normally blocks the N-methyl-D-aspartate (NMDA) receptors in the post-synaptic membrane.[7] Nociceptive pain and mild inflammatory pain signals (ie, action potentials) primarily activate the AMPA receptors on the postsynaptic membrane. When increased numbers of action potentials reach the postsynaptic membrane and a critical number of AMPA receptors are activated, the postsynaptic membrane is depolarized, allowing the extrusion of the magnesium plug in the NMDA receptor. AMPA receptors allow sodium and potassium to enter the cell, NMDA receptors allow sodium,

potassium and calcium to enter.[7,8] The entrance of calcium amplifies pain through a variety of mechanisms, including the release of arachidonic acid.[7,8]

A major criticism of the treatment protocol is that analgesia was not administered when the other treatments started. The dog did respond to abdominal palpation by tensing and whimpering, both signs of pain, and the dog did have a disease known to cause pain. However, the admitting veterinarian felt that the pain was minor and might resolve without analgesia. At the first-recheck after initiating therapy, the attending veterinarian felt that analgesia was definitely necessary. The pain may have worsened since the time of admission since peripheral and central sensitization were likely occurring. Untreated pain is not only a welfare and quality of life issue, it is also a health issue. For example, pain can cause delayed healing through increased cortisol release and immunosuppression, which could have negatively impacted this patient if pain had not been addressed early.

Another potential criticism is that buprenorphine was decreased to BID for the last 24 hours but buprenorphine-mediated analgesia is unlikely to last 12 hours. However, this was done to wean the treatments down while watching for break-through pain while the dog was still in the hospital.

Not pain related but a potential concern could be the use of antibiotics since this is a viral disease but antibiotics are administered in patients with GE because bacteria are often translocated from the intestinal lumen across the denuded mucosa and into the blood stream. In addition, CPV causes leukopenia. These combine to put the patient at increased risk of bacteremia.

The pain scale used, CMPS-SF, is a widely-used ‘multi-item behavioral pain assessment tool, developed and validated using a psychometric approach, to measure acute pain in the dog’.[1,9]

While often described as ‘validated for recognition and assessment for acute postoperative pain’, the developer says simply ‘acute pain’, thus we use if for a variety of pain conditions. The scale includes six behavioral categories with descriptors: vocalization, attention to wound, mobility, response to touch, demeanor and posture/activity.[1,9] To ensure accuracy, validated scales should be used as researched. We omitted the section on rises/walks because the dog was restricted to its cage since it had a highly contagious disease. Fortunately, the CMPS-SF was validated with and without that section, likely because the most common use of the scale is for assessment of postoperative pain,[9] including pain from orthopedic procedures that may preclude rising/walking in the immediate post operative period. When the section on rises/walks is omitted, the score to treat becomes 5/20 (20 total points) rather than 6/24. The CMPS-SF is a very easy scale to incorporate into a pain assessment program.

Our treatment protocol included lidocaine infusions, which have been used for a wide variety of pain syndromes, including visceral or abdominal pain, in humans[10] and horses.[11] Although not all studies have the same outcome, horses, especially those recovering from abdominal surgery, tend to have decreased postoperative pain scores and increased gastrointestinal motility if a lidocaine infusion was part of the intraoperative analgesic protocol.[12] Lidocaine infusions did not increase motility in dogs with normal motility[13] but has not been studied in dogs with slowed motility or ileus. Lidocaine infusions decreased the need for intraoperative fentanyl in dogs undergoing soft tissue or orthopedic surgery.[14] Our clinical impression based on pain scoring is that lidocaine does contribute to analgesia, but obviously more research is needed. We have not evaluated motility. The analgesic effects of IV lidocaine are not thoroughly understood but include a central rather than a local site of action[15,16] and an anti-inflammatory effect due to inhibition of neutrophils.[12] As for adverse effects, lidocaine infusions at can cause sedation, nausea and

vomiting[17] and overdose by any route of administration can cause muscle fasciculations, coma and death.[18]

An opioid (buprenorphine) was also administered to this patient. Opioids have analgesic activity both in the transmission ('spinal') and perception ('supraspinal') steps of the pain pathway.[19] Opioids bind to the mu and kappa endogenous G-protein coupled receptors both presynaptically and postsynaptically. Binding to presynaptic receptors causes a blockade of presynaptic calcium channels, which decreases the release of nociceptive neurotransmitters like substance P and glutamate. Binding to postsynaptic G-protein coupled receptors causes postsynaptic potassium channels to open, thus hyperpolarizing cell membranes and increasing the strength of the action potential required to transmit the nociceptive signal. Opioids can cause sedation, nausea and vomiting so could potentially exacerbate some of the adverse effects of the GE. Opioids can also slow GI motility, which is sometimes, but not always, desired in patients with hypermotility. However, buprenorphine, a partial-mu receptor agonist, is moderately potent and less likely than full mu-agonist opioids to cause these adverse effects.[20]

Maropitant may have also contributed to analgesia. Maropitant is a neurokinin-1 (NK-1) receptor antagonist, which prevents substance P, a potent pain mediator, from binding to the NK-1 receptor.[20] Since this occurs in both the emetic and pain pathways, it has been suggested that 'NK-1 receptor antagonists might be effective for managing visceral pain'.[21] In addition, the 'strong expression of NK-1 immunoreactivity' in ileal muscle and mucosal immune cells from dogs with spontaneous ileal inflammation compared to the same cells from dogs without ileal inflammation 'may provide a rationale for the use of NK-1 antagonist drugs in the treatment of intestinal inflammation'.[21] Although not visceral pain, studies of anesthetized dogs show that

maropitant decreases the dose of inhalant (or reduced minimum alveolar concentration [MAC]) required to maintain anesthesia in patients undergoing a research model of pain.[23]

Other analgesic treatment options might include NSAIDs since the pain is in large-part inflammatory but NSAIDs are often omitted since they can cause GI ulceration and could potentially exacerbate the GE pathology. However, some veterinarians anecdotally advocate their limited use (eg, generally one dose). NSAIDs should only be administered after the patient has been rehydrated since NSAID-related renal damage would be more likely to occur in the in dehydrated patient. Steroids have been anecdotally used to control intestinal pain and inflammation from GE. Ketamine, an NMDA-receptor antagonist, could be used as an IV infusion to decrease pain from central sensitization. Acupuncture and other nonpharmacologic treatments should also be considered.

The duration of therapy was based on decreasing pain scores and overall wellbeing of the dog. The dog was not expected to be painful after resolution of the disease so no analgesics were dispensed for at-home administration.

Summary

Visceral pain can be as severe as somatic pain but it often seems to be overlooked, or at least underestimated in veterinary patients. Visceral disease or conditions that cause pain in humans, like gastroenteritis, should be expected to cause pain in animals. In addition, pain scoring should be used in animals with expected all painful diseases and not limited to postsurgical pain. With anticipation of pain based on disease pathologic and assessment of pain using validated pain scores, veterinary professionals are more likely to be able to prevent/control pain. Pain relief is

important for the patient's health, behavior, welfare and quality of life. In this case visceral pain from canine parvovirus-induced gastroenteritis was controlled with a combination of intravenous lidocaine and buprenorphine. In this patient, a pain scale validated for identification of acute pain was used to assess pain and to dictate not only efficacy of pain control but also duration of treatment.

References

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