Intra- and postoperative opioid-sparing analgesia in a cat undergoing pelvic limb amputation

Francesco Santoro[1] iD**, Diego Castineiras[2] and Johanna Kaartinen[1]**

Abstract

Case summary A combination of preoperative epidurally administered morphine, peripheral nerve blocks and postoperative wound irrigation with ropivacaine is described as an opioid-sparing analgesic protocol for a feline immunodeficiency virus-positive cat with hypertrophic cardiomyopathy undergoing hindlimb amputation. The reported strategy resulted in a lack of intraoperative sympathetic response, haemodynamic stability and adequate postoperative analgesia. No rescue analgesia was needed at any point.
Relevance and novel information This report represents an example of how several locoregional techniques can be effectively combined to minimise the perioperative use of systemic opioids and their potential side effects in selected cases.

Keywords: Analgesia; regional anaesthesia; chronic pain; limb amputation

Case description

A 7-year-old domestic shorthair male neutered cat was admitted to the Queen Mother Hospital for Animals for the presence of a soft-tissue sarcoma at the level of the right tarsus. The cat had a 2-year history of hypertrophic cardiomyopathy (with dynamic left outflow tract obstruction and normal left atrial size) and was feline immunodeficiency virus (FIV) positive. An informed consent form for sedation/anaesthesia, and diagnostic and surgical procedures was signed by the owner prior to admission.

CT and abdominal ultrasound scan were performed as part of a full oncological staging, and revealed no obvious evidence of metastatic disease. Haematology and serum biochemistry were also performed and showed mild leukopenia (4.51×10^9/l; reference interval [RI] 5.5–19.5), lymphopenia (0.54×10^9/l; RI 1.5–7), mild non-regenerative anaemia (haematocrit 23.4%; RI 24–45%; haemoglobin 7.6 g/dl; RI 8–15), mild hypoalbuminaemia (23.7 g/l; RI 25–45), and a mild increase in alanine transaminase (80 U/l; RI 5–60) and creatine kinase (613 U/l; RI 57–574). Considering these findings, a right hindlimb amputation was advised and performed.

When examined before the general anaesthesia, the cat was bright and alert; heart rate was 200 beats/min (bpm); respiratory rate was 20 breaths/min; mucous membranes were pink, with a capillary refill time <2s; body condition score was 6/9; and body temperature was within normal limits. At auscultation of the thorax, a left systolic grade 4/6 heart murmur was detected, and the lung fields were unremarkable. The night before surgery a 22G peripheral venous catheter was placed in the left cephalic vein, and routine preoperative fasting was observed.

[1]Department of Clinical Sciences and Services, The Royal Veterinary College, Hatfield, UK
[2]Willows Veterinary Centre & Referral Service, Solihull, Birmingham, UK

Corresponding author:
Francesco Santoro DVM, MRCVS, Department of Clinical Sciences and Services, The Royal Veterinary College, Hawkshead Lane, Hatfield AL9 7TA, UK
Email: doc.tabarez@gmail.com

The following morning, the cat was premedicated with methadone (0.2 mg/kg) and dexmedetomidine (0.002 mg/kg) intravenously (IV) and anaesthesia was induced with alfaxalone (1 mg/kg) IV 20 mins later. After lidocaine was sprayed on the laryngeal arytenoid cartilages, the trachea was intubated with a 4.5 cuffed plastic tube, and the cuff was inflated enough to prevent air leakage during gentle positive pressure ventilation. The endotracheal tube was then connected to a Mapleson D (modified paediatric T-piece) type breathing circuit and isoflurane was delivered in 100% oxygen to maintain general anaesthesia. The cat was immediately connected to a multiparametric monitor (S5; Datex Ohmeda) and electrocardiogram; peripheral oxygen saturation, non-invasive blood pressure, respiratory rate, end-tidal carbon dioxide and isoflurane concentrations, inspired fraction of oxygen and oesophageal temperature were recorded every 5 mins until the end of general anaesthesia. Hartmann's solution was started at a rate of 3 ml/kg/h, and active warming was provided with a heat pad (HotDog; Augustine Surgical) during the preparation phase, and with a forced air blanket (Bair Hugger; 3M) during the surgery. After trichotomy and aseptic preparation of the surgical field, a combination of different locoregional techniques was performed.

A sacrococcygeal peridural injection of preservative-free morphine sulfate (0.1 mg/kg) diluted in 0.2 ml/kg of sterile normal saline was performed with the cat in sternal recumbency, localising the space via a lack of resistance to sterile saline injection. Subsequently, using previously reported locoregional techniques,[1] an ultrasound-guided right sided psoas compartment and parasacral block were performed by injecting 1 ml of ropivacaine 0.5% into each site (total volume 2 ml; total dose 2 mg/kg). For the psoas compartment block a 13-6 MHz linear transducer (SonoSite SII; Fujifilm) was positioned immediately cranial to the iliac crest, with the linear ultrasonographic probe perpendicular to the vertebral column and directed dorsomedially in order to visualise the psoas major muscle and the femoral and obturator nerves running within it. A 5 cm echogenic single shot nerve block needle (Ultraplex; B Braun) was advanced in plane with the ultrasonographic beam, from the dorsal margin of the acoustic window, until its tip was seen adjacent to the target nerve structures. For the parasacral block, the ultrasound probe was placed on the gluteal region, perpendicular to the spine, at the level of the greater sciatic notch, and the lumbosacral trunk was visualised medially adjacent to the ileum. The needle was then advanced in plane with the transducer in a mediolateral direction, until its tip was seen adjacent to the nerves. After negative aspiration, perineural administration was performed and spread of the local anaesthetic was visualised after injection of 1 ml at both sites.

The cat was then transferred to the operating room, positioned in left lateral recumbency and connected to an anaesthesia workstation (Aestiva/5; Datex Ohmeda) and monitor (Carescape B650; GE Healthcare). Intermittent positive pressure ventilation was started, using pressure control to deliver a tidal volume of 10 ml/kg (peak inspiratory pressure 6–8 cmH$_2$O) and with a respiratory rate of 14–16 breaths/min, in order to maintain normocapnia.

The amputation was performed by coxofemoral disarticulation, and before the subcutaneous layer was reconstructed, a 4 inch (~10 cm) fenestrated wound diffusion catheter (MILA International) was advanced through a small skin incision and sutured in place, in order for it to lie between the muscular and cutaneous layers.

During the 80 mins of surgery, median heart rate was 90 bpm (range 85–105); median systolic blood pressure (BP) was 85 mmHg (range 80–95), median mean arterial BP was 65 mmHg (range 60–80) and median diastolic BP was 55 mmHg (range 35–70) mmHg; median core body temperature was 34.8°C (range 34.4–35.7); and median end-tidal isoflurane was 1.1% (range 1.0–1.2%). A single dose of glycopyrronium (10 µg/kg IV) was administered 10 mins before the first incision due to bradycardia with an associated mean arterial BP <60 mmHg. Two doses of cefuroxime (20 mg/kg IV) were administered (one preoperatively and one intraoperatively) as part of the standard surgical antibiotic prophylactic therapy. No vasoactive or rescue analgesic drugs were required at any stage during the procedure. The perioperative use of non-steroidal anti-inflammatory drugs (NSAIDs) was discussed within the team. As the cat had recent history of a gastrointestinal adverse reaction to meloxicam, and considering a possible postanaesthetic deterioration of the cardiovascular function, the clinician in charge of the case decided to avoid this class of drugs.

After surgery, a rigid buster collar was placed, and the cat was transferred to the anaesthesia recovery suite and into an incubator until restoration of normothermia. An infusion of Hartmann's solution at 2 ml/kg/h was continued until the cat was able to drink and eat voluntarily.

The postoperative analgesic plan included bupivacaine 0.25% (diluted with sterile sodium chloride 0.9% [total dose 2 mg/kg, total volume 4.4 ml]) injection through the wound infusion catheter every 6 h. The first dose was administered 5 h after the execution of the preoperative nerve blocks.

Postoperative pain was assessed and scored using a modified version of the Colorado State University Veterinary Medical Center (CSUVMC) Feline Acute Pain Scale. The final score was the result of the evaluation of three components: body tension; psychological and behavioural changes; and response to palpation. Each component ranged from 0 to 4 (minimal to severe

pain). Rescue analgesia with methadone (0.2 mg/kg IV q4h) was planned in case of a total score exceeding 4/12. Postoperative pain was assessed every 2 h for the whole hospitalisation period, starting from the post-extubation period, as soon as the cat was deemed conscious (alert, responsive, aware of the surrounding environment, capable of lifting its head).

The wound catheter was kept in place for 5 days. During the first 4 days, the aforementioned dose regimen of bupivacaine was followed. On the fifth post-operative day, bupivacaine was administered based on pain scores, evaluated hourly after the last administration. Since the pain score was still below the intervention threshold 12 h after the last bupivacaine bolus, the wound catheter was removed, and the cat discharged.

No sedation or analgesia were needed for the wound catheter removal, and no rescue dose of methadone was required during the entire postoperative period. Based on the absence of detectable pain during the last 12 h of hospitalisation, the cat was discharged without any analgesic prescription. The owner was instructed to record any sign of pain such as muscular twitching at the level of the stump, restlessness and continuous changing of position, looking at/licking/biting/scratching the wound, preferring to lie on a cold surface, anxiety, inappetence, tendency to remain isolated, reluctance to move, aggressiveness and pain-related facial expression. If any of the aforementioned signs were noted, the owner was asked to inform the clinician in charge as soon as possible so that further administration of analgesics at home (eg, oral gabapentin) could be considered.

At a 10-day follow-up, the owner reported the cat being comfortable and subjectively pain-free, and the surgical wound healed without complications.

Discussion

This report represents an example of opioid-sparing analgesia in a cat undergoing pelvic limb amputation.

Although analgesic properties of opioids are well known, these drugs are often associated with side effects such as perioperative nausea and vomiting, gastro-oesophageal reflux and regurgitation, dysphoria, sedation, hyperalgesia, reduction of gastrointestinal motility, immune suppression, and, in people, a high risk of addiction and abuse.[2-4] Many of these undesired effects may have a negative impact on the patient's outcome. In fact, several systematic reviews and guidelines focused on the perioperative wellbeing of the hospitalised patients found several benefits in a reduced administration, or sometimes complete avoidance, of opioids, and the use of locoregional analgesia.[5,6]

Most of the side effects related to full mu-agonist opioids administration have also been described in cats, although their clinical impact is still to be clarified.[2]

From the point of view of the anaesthetists in charge of the case reported here, apart from the common anaesthesia-related complications, the main concerns were somatic and neuropathic pain, peri- and intra-operative cardiovascular stability and immune function.

Neuropathic pain and phantom limb pain induced by surgical nerve damage is among the frequent complications of limb amputations in people.[7] Signs attributable to chronic pain are common after limb amputation surgery in cats,[8] and phantom limb pain has been described in this species in a recent case report.[9] While in humans the use of perioperative locoregional anaesthesia can been associated with a lower incidence of post-amputation/postoperative chronic pain,[10] similar data are currently unavailable in cats. Furthermore, a validated pain scale for the detection of post-amputation pain in cats has not yet been developed. The signs of pain the owner was asked to report after the cat was discharged were the result of a recent study investigating the most common behavioural changes observed for months after limb amputation in cats.[11]

NSAIDs such as meloxicam are licensed analgesic drugs in cats and have been proven effective in treating post-operative pain after ovariohysterectomy[12] and orthopaedic surgeries.[13] Their side effects include gastro-intestinal ulceration and impairment of renal blood flow autoregulation in cases of hypovolemia and/or hypotension. However, the adverse renal effects are species- and drug-specific, and COX-1 and COX-2 enzyme expression and distribution in feline kidney remain unknown. Judicious use of NSAIDs in feline patients should thus be performed, although a single dose in healthy cats appears to be clinically safe.[14] In cats with hypertrophic cardiomyopathy, congestive heart failure can develop after a general anaesthesia,[15] thus compromising global systemic perfusion. Although NSAIDs can be considered first-choice drugs in an opioid-sparing protocol, considering this latter reported risk, and given the cat's history of adverse gastrointestinal signs related to meloxicam administration, the clinical team opted against their use.

To provide intra-and postoperative analgesia, reducing the stress response and the associated haemodynamic changes, a combination of several locoregional techniques was adopted.

Peridural administration of morphine has shown the potential for long-lasting postoperative analgesia (up to 10–12 h) in dogs and cats undergoing various types of surgical procedures.[16] The combination of peripheral nerve blocks used in this report has already been described as an effective analgesic strategy for a cat undergoing the same procedure.[1] Adding a local anaesthetic to the epidural injection could have been a quicker and simpler analgesic option. Nevertheless, the resulting

sympathetic blockade could have led to hypotension,[17] necessitating treatment with drugs potentially negatively affecting systolic or diastolic function and increasing myocardial oxygen demand, thus resulting in haemodynamic instability and myocardial stress.

Furthermore, the use of wound diffusion catheters has been reported in cats as an effective strategy for several days of continuous postoperative analgesia.[18] The total dose of bupivacaine and the dosing interval used for this case were chosen to minimise the likelihood of toxic plasmatic concentrations and relative clinical effects.

In cats infected with FIV, stress reduction has always been considered an important aspect.[19] Compared with opioid-based systemic analgesia, locoregional anaesthesia is associated with a lower level of stress response during the intra- and postoperative periods, as proven in several species, including dogs.[20] The immunomodulatory effects of opioids have additionally been demonstrated in cats,[3] although other non-opioid analgesic and anaesthetic agents have also shown potential for immune suppression.[21]

Perioperative control of the stress response and a reduced sympathetic system outflow may be desirable factors in cats affected by hypertrophic cardiomyopathy, in order to increase the diastolic filling time, decrease the dynamic stenosis of the left outflow tract and avoid a higher myocardial oxygen consumption.[22]

Conclusions

The opioid-sparing anaesthetic protocol described in this report resulted in a lack of intraoperative sympathetic response, haemodynamic stability and adequate postoperative analgesia in an FIV-positive cat with hypertrophic cardiomyopathy undergoing hindlimb amputation. Although some of the clinical advantages of a similar protocol are still to be demonstrated (especially reduction of the stress response and a lower degree of immune depression), this report represents an example of combining several locoregional techniques to minimise the perioperative use of systemic opioids and their potential side effects for selected cases.

ORCID iD Francesco Santoro (iD) https://orcid.org/0000-0003-4037-152X

References

1 Trujanovic R, Otero PE and Larenza Menzies MP. **Combined ultrasound/electrostimulation-guided block of the lumbosacral plexus in a cat undergoing pelvic limb amputation.** *Vet Rec Case Rep* 2020; 8: 1–5.

2 Bortolami E and Love EJ. **Practical use of opioids in cats: a state-of-the-art, evidence-based review.** *J Feline Med Surg* 2015; 17: 283–311.

3 Odunayo A, Dodam JR, Kerl ME, et al. **State-of-the-art-review: immunomodulatory effects of opioids.** *J Vet Emerg Crit Care* 2010; 20: 376–385.

4 Deyo RA, Hallvik SE, Hildebran C, et al. **Association between initial opioid prescribing patterns and subsequent long-term use among opioid-naïve patients: a statewide retrospective cohort study.** *J Gen Intern Med* 2017; 32: 21–27.

5 Wainwright TW, Gill M, McDonald DA, et al. **Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations.** *Acta Orthopaedica* 2020; 91: 3–19.

6 Nelson G, Bakkum-Gamez J, Kalogera E, et al. **Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations – 2019 update.** *Int J Gynecol Cancer* 2019; 0: 1–18.

7 Limakatso K, Bedwell GJ, Madden VJ, et al. **The prevalence and risk factors for phantom limb pain in people with amputations: a systematic review and meta-analysis.** *PLoS One* 2020; 15: e0240431. DOI: 10.1371/journal.pone.0240431.

8 Forster LM, Wathes CM, Bessant C, et al. **Owners' observations of domestic cats after limb amputation.** *Vet Rec* 2010; 167: 734–739.

9 O'Hagan BJ. **Neuropathic pain in a cat post-amputation.** *Aus Vet J* 2006 84: 83–86.

10 Humble SR, Dalton AJ and Li L. **A systematic review of therapeutic interventions to reduce acute and chronic post-surgical pain after amputation, thoracotomy or mastectomy.** *Eur J Pain* 2015; 19: 451–465.

11 Menchetti M, Della Rocca G, Tartari I, et al. **Approaching phantom complex after limb amputation in cats.** *J Vet Behav* 2022; 50: 23–29.

12 Slingsby LS and Waterman-Pearson AE. **Postoperative analgesia in the cat after ovariohysterectomy by use of carprofen, ketoprofen, meloxicam or tolfenamic acid.** *J Small Anim Pract* 2000; 41: 447–450.

13 Murison PJ, Tacke S, Wondratschek C, et al. **Postoperative analgesic efficacy of meloxicam compared to tolfenamic acid in cats undergoing orthopaedic surgery.** *J Small Anim Pract* 2010; 51: 526–532.

14 Lascelles BD, Court MH, Hardie EM, et al. **Nonsteroidal anti-inflammatory drugs in cats: a review.** *Vet Anest Analg* 2007; 34: 228–250.

15 Rush JE, Freeman LM, Fenollosa NK, et al. **Population and survival characteristics of cats with hypertrophic cardio-myopathy: 260 cases (1990–1999).** *J Am Vet Med Assoc* 2002; 220: 202–207.

16 Troncy E, Junot S, Keroack S, et al. **Results of preemptive epidural administration of morphine with or without bupivacaine in dogs and cats undergoing surgery: 265 cases (1997–1999).** *J Am Vet Med Assoc* 2002; 221: 666–672.

17 Taniguchi M, Kasaba T and Takasaki M. **Epidural anesthesia enhances sympathetic nerve activity in the unanesthetized segments in cats.** *Anest Analg* 1997; 84: 391–397.

18 Abelson AL, McCobb EC, Shaw S, et al. **Use of wound soaker catheters for the administration of local anesthetic for post-operative analgesia: 56 cases.** *Vet Anest Analg* 2009; 36: 597–602.

19 August JR. **Husbandry practices for cats infected with feline leukemia virus or feline immunodeficiency virus.** *J Am Vet Med Assoc* 1991; 99: 1474–1477.

20 Romano M, Portela DA, Breghi DA, et al. **Stress-related biomarkers in dogs administered regional anaesthesia or fentanyl for analgesia during stifle surgery.** *Vet Anest Analg* 2016; 43: 44–54.

21 Hernandez-Avalos I, Flores-Gasca E, Mota-Rojas D, et al. **Neurobiology of anesthetic-surgical stress and induced behavioral changes in dogs and cats: a review.** *Vet World* 2021; 14: 393–404.

22 Kittleson MD and Côté E. **The feline cardiomyopathies 2. Hypertrophic cardiomyopathy.** *J Feline Med Surg* 2021; 23: 1028–1051.