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RESEARCH PAPER

# Comparison of intratesticular lidocaine, sacrococcygeal epidural lidocaine and intravenous methadone in cats undergoing castration: a prospective, randomized, investigator-blind clinical trial

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Running head: Locoregional anaesthesia or methadone in cats

**Abstract**

**Objective** The objective of this study was to compare three analgesic protocols for feline castration.

**Study design** Prospective, randomized clinical study.

**Animals** Forty-nine client-owned cats.

**Methods** Cats were injected intramuscularly with dexmedetomidine (15 µg $kg^{-1}$) and alfaxalone (3 mg $kg^{-1}$) and assigned randomly to one of three treatment groups. Group ITL (n = 15) received intra-testicular 2% lidocaine (0.05 ml each testicle), group SCL (n = 15) a sacro-coccygeal epidural injection of 2% lidocaine (0.1 mL $kg^{-1}$), and group IVM (n = 19) intravenous methadone (0.3 mg $kg^{-1}$), before surgery. Cardiorespiratory variables were recorded. In case of autonomic nociceptive response, intravenous fentanyl (2 µg $kg^{-1}$) was administered. During recovery, time from intramuscular atipamezole (75 µg $kg^{-1}$, administered at the end of surgery) to sternal recumbency and to active interaction was recorded. Quality of recovery was assessed with a simple descriptive scale (SDS). Postoperative analgesia was evaluated with a visual analogue scale (VAS) and the UNESP-Botucatu multidimensional composite pain scale (MCPS) at return of active interaction and then 1, 2 and 3 hours later.

**Results** The three analgesic protocols were comparable in terms of intraoperative fentanyl and propofol requirement. Cardiorespiratory variables stayed within normal ranges in the majority of the cases, although group IVM had the lowest intraoperative respiratory rate ($p$ = 0.0009).

No significant differences were detected between groups in UNESP-Botucatu MCPS scores ($p$ = 0.21). However, group ITL showed higher VAS score than group IVM ($p$ = 0.001). Four cats enrolled in group ITL, as well as three of group SCL and one of group IVM, required rescue analgesics before the completion of pain assessment.

**Conclusion and clinical relevance** Intratesticular and sacrococcygeal epidural lidocaine injections could be regarded as good alternatives to systemic opioids in cats undergoing castration, although the benefits of these techniques seem to be of shorter duration than intravenous methadone.

## Introduction

Neutering of client-owned cats is a common procedure in veterinary practice. Traditionally, when performing castration of male cats the majority of French veterinarians prefer injectable anaesthetic techniques to inhalation anaesthesia. The reasons behind this choice may be a lack of familiarity with feline tracheal intubation, as well as the potential for complications associated with this procedure (Brodbelt et al. 2007).

Ideally, an intramuscular (IM) anaesthetic protocol for castration should be safe for the animal, inexpensive, and provide reliable unconsciousness, muscle relaxation and analgesia. Combinations of alpha 2-adrenoreceptor agonists, induction agents suitable for IM administration and opioids are used for this purpose (Adami et al. 2015).

Systemic full μ-opioid agonists are commonly employed to provide perioperative analgesia. Unfortunately, they are controlled drugs and their use requires detailed record keeping; a drawback which can prevent practitioners from using them on a regular basis (Hugonnard et al. 2004). As an alternative to systemic analgesia, locoregional anaesthesia is becoming increasingly popular in veterinary medicine, and its use is widespread not only by board-certified anaesthetists, but also between general practitioners.

Intratesticular injection of local anaesthetics has been successfully used to provide perioperative analgesia for castration in dogs (Huuskonen et al. 2012), piglets (Haga et al. 2006a), horses (Haga et al. 2006b), alpacas (Nickell et al. 2015) and people undergoing testicular biopsies (Kamal et al. 2002).

Sacrococcygeal epidural injection of lidocaine is widely used in horses and ruminants to desensitize the perineum and the pelvic organs without a loss of motor function of the pelvic limbs. This technique has also been reported to relieve the pain associated with urethral catheterization in cats with an onset of action of about five minutes (O'Hearn et al. 2011). Both intratesticular and sacrococcygeal epidural injections of local anaesthetics may be used to desensitize the testicles and the spermatic cord in cats.

The aim of this study was to compare three analgesic protocols: systemic administration of methadone, sacrococcygeal epidural lidocaine, and intratesticular lidocaine injection, in terms of quality and duration of analgesia in male cats undergoing castration.

Our hypothesis was that the three protocols would result in comparable propofol requirements and quality of intraoperative analgesia in cats undergoing elective castration.

## Materials and methods

### Animals

Forty-nine client-owned male cats undergoing elective castration were included in the study. The number of participants was established on the basis of a sample size calculation using a commercial software program (SigmStat and SigmaPlot 12). It was performed by setting the power at 80%, the level of significance at 5% and the end point as a postoperative Visual Analogue Scale (VAS) pain score difference between groups of 10 mm with a standard deviation of 5 mm.

Cats underwent a routine preanaesthetic physical examination in order to assess the health status. Exclusion criteria were: presence of systemic disease, impaired cardiovascular function, and age above 8 years. Food, but not water, was withdrawn 12 hours prior to surgery. The study was performed under approval of the ethical committee of the Faculty of Veterinary Medicine of Alfort, France, and informed owner consent.

**Procedures**

All cats were injected IM into the dorsolumbar muscles with dexmedetomidine (15 µg $kg^{-1}$) (Dexdomitor; Orion Pharma, Finland) and alfaxalone (3 mg $kg^{-1}$) (Alfaxan; Jurox, Australia) by the anaesthetist in charge for evaluating intraoperative nociception, depth of anaesthesia, postoperative pain and quality of recovery. The drugs were combined in the same syringe and if the total injection volume exceeded one mL, it was split into two injection sites. The doses were established on the basis of previous pilot work.

The times from injection to sternal recumbency (defined as a position with the pelvic limbs tucked under the body) and to lateral recumbency (defined as the cats lying on the side) were recorded, as well as the time of induction of general anaesthesia. The latter was defined as absence of righting reflex when the cats were positioned in dorsal recumbency, and unresponsiveness to vocal and tactile stimulation. If general anaesthesia was not induced 30 minutes after the injection, the cats were injected IM with half of the initial doses of both dexmedetomidine and alfaxalone, and excluded from the study.

Vomiting, hypersalivation, tremors, myoclonus and/or increased muscular tone were considered adverse events and were recorded. After induction of anaesthesia, a 22 gauge catheter (Delta Med, Italy) was placed in one cephalic vein. All cats received 7 mL $kg^{-1}$ $hour^{1}$ intravenous crystalloids (NaCl 0.9%; B. Braun, Germany) during the anaesthetic. Amoxicillin (Clamoxyl; GlaxoSmithKline, UK), 20 mg $kg^{-1}$, was administered IV 30 minutes before the start of surgery. A multiparametric module (Monitor BSM-2301K; Nihon Kohden, Japan) was used to monitor cardiorespiratory variables. Electrocardiography was used to detect heart rate (HR), visual observation of the chest movements to detect respiratory rate ($f_R$), pulse oximetry for pulse rate and arterial oxygen saturation ($SpO_2$), and oscillometry to measure systolic, mean and diastolic arterial pressures (SAP, MAP and

DAP). An appropriate size cuff (width equal to 40% of limb circumference) was placed over the radial artery.

The cats breathed room air. When intraoperative HR was lower than 100 beats minute$^{-1}$ atipamezole (75 µg kg$^{-1}$, Alzane, Zoetis, NJ, USA) was administered IM, and the cats were excluded from the study. Cats with $f_R$ < 6 breaths minute$^{-1}$ required endotracheal intubation to allow manually assisted ventilation, and were excluded from the study. Hypotension, defined as MAP values below 60 mmHg, was treated with a 3 ml kg $^{-1}$ bolus of crystalloids. If the fluid bolus failed to increase the MAP above the cut-off value of 60 mmHg, the crystalloid's rate of infusion was increased to 10 ml kg$^{-1}$ h$^{-1}$. Unresponsive hypotension was treated with a bolus of hydroxyethyl starch (5 ml kg$^{-1}$; Voluven 6%, Fresenius Kabi, France). If hypotension still persisted and the anaesthesist considered the administration of vasopressors or anticholinergic appropriate, then the cats were excluded from the study. Animals with $SpO_2$ values below 94% received supplemental oxygen at a rate of 2 L minute$^{-1}$, delivered via face mask. If $SpO_2$ failed to normalize, endotracheal intubation was performed to allow manually assisted ventilation and administration of 100% oxygen, and the cats were excluded from the study. If during the anaesthetic the rectal body temperature decreased below 36.5 ºC, a forced air warmer (Warm Touch, Mallinckrodt Medical, Ireland) was used.

The end of surgery was defined as completion of the last suture knot (deferens and/or blood vessels), at which time atipamezole was administered IM (75 µg kg$^{-1}$, Alzane, Zoetis, NJ, USA). Times to sternal recumbency and to active interaction (defined as responsiveness to vocal calls, alertness and interest in the surrounding), were recorded.

At the end of the assessments (T8; Fig. 1), 0.2 mg kg$^{-1}$ subcutaneous meloxicam (Metacam, Boerhinger-Ingelheim, Germany) was administered to all cats. Subcutaneous buprenorphine

(20 µg $kg^{-1}$) was administered to all cats who had no prior buprenorphine administered as a rescue analgesic.

**Treatment groups**

The cats were randomly assigned to receive one of three treatments. A manual randomization technique, based on drawing pieces of paper from an envelope, was used. Group ITL received 2% lidocaine at a volume of 0.05 mL $kg^{-1}$ per testicle. Gentle aspiration before injection was used to exclude intravenous needle placement. Group SCL received a sacrococcygeal epidural injection of 2% lidocaine, at the dose of 2 mg $kg^{-1}$, corresponding to a volume of 0.1 mL $kg^{-1}$. Lack of resistance to injection and subsequent relaxation of the anal sphincter were used to confirm the correct location of the epidural injection. Group IVM received an intravenous (IV) injection of methadone at the dose of 0.3 mg $kg^{-1}$.

All the analgesic treatments (either one of the two locoregional techniques or the systemic administration of methadone) were performed five minutes before the surgical incision, by a co-investigator not involved in the assessments. In order to prevent the primary investigator from recognizing the treatment group, the sacrococcygeal area was clipped and surgically prepared in all the cats enrolled in the study.

**Intraoperative evaluation of nociception**

All the assessments were carried out by the primary investigator who was unaware of the treatment allocation. The surgeries were performed by junior clinicians under the supervision of a senior surgeon. Depth of anaesthesia was evaluated based on the following descriptors: spontaneous blinking (yes or no); movements during surgical stimulation (yes or no); and adequate muscle relaxation (yes or no). If depth of anaesthesia was too light the cat received propofol (0.5 mg $kg^{-1}$ IV) (Propovet; Abbot, UK).

For each cat, baseline values for HR, $f_R$ and MAP were established after induction of anaesthesia and before surgical stimulation (T0, baseline values). The above listed variables were then measured and recorded at the following time points: first surgical incision (T1), traction of the first testicle (T2), second surgical incision (T3) and traction of the second testicle (T4). Intraoperatively, any increase in two of three parameters (HR, $f_R$ or MAP) of 30% above baseline was considered indicative of nociception. When such an increase was observed for at least two of the three physiological variables, 2 µg $kg^{-1}$ fentanyl (Fentanyl Mylan 50 µg $ml^{-1}$, PA, USA) was administered IV. The requirement for fentanyl during surgery was used to evaluate intraoperative antinociception.

**Assessment of postoperative pain and quality of recovery**

After atipamezole injection, a simple descriptive scale for the assessment of recovery quality was used with (0) defined as a very smooth recovery, (1) a smooth recovery, (2) a poor recovery and (3) a very poor recovery, as soon as the cats regained sternal recumbency.

Postoperative pain was evaluated with a VAS, where 0 mm was labelled as “no pain” and 100 mm as “worst possible pain” (Jensen et al. 2003). Additionally, a modified version of the UNESP-Botucatu MCPS (Brondani et al. 2013) was used. The subscale named “physiological change” was excluded from the evaluation so that the maximum total score was 24 (severe pain) instead of 30. Pain assessments were performed during recovery, when the cats were observed to interact actively (T5) with the investigator, and then 1 (T6), 2 (T7) and 3 (T8) hours later as shown in Fig. 1. The intervention levels for administration of additional analgesia (buprenorphine 20 µg $kg^{-1}$ IV, Vetergesic, Sogeval, France) were the following: a score greater than 2 for the descriptor “expression of pain”, or a score greater than 3 for the descriptor “psychomotor changes” on the UNESP-Botucatu MCPS, or a score exceeding 40 mm on the VAS.

The post-operative pain assessments were carried out by the same investigator who evaluated intraoperative nociception and who was unaware of the treatment allocation.

**Statistical analysis**

Data are presented as means ± standard deviation or as medians (range) where applicable. Normality of data distribution was assessed with the Shapiro-Wilk test and with the Kolmogorov-Smirnov test. Age, body weight, number of propofol and fentanyl boluses administered intraoperatively in each group, and time from atipamezole injection to recovery were analyzed with a non-parametric test (Kruskal Wallis test, followed by Kruskal-Wallis multiple comparison Z value test). Repeated measures ANOVA, followed by Tukey Kramer's multiple comparison test, was used to compare the intraoperative physiological variables (HR, $f_R$ and MAP), as well as the postoperative pain scores, between treatments and between time points. Duration of anaesthesia and time to active interaction were analysed with a one-way ANOVA, followed by Bonferroni multiple comparison test. The Fisher exact test was used to compare the number of animals within each group requiring rescue buprenorphine before the completion of the last pain assessment. Statistical analyses were performed using commercially available software (NCSS, 2007). Values of $p < 0.05$ were considered statistically significant.

**Results**

Fifty-four cats were considered possible candidates for the study, but seven were excluded due to their fractious nature. A total of 49 cats, which were aged 8 (5 – 18) months and weighed 3.8 (2.2 - 6.5) kg, were included. Treatment groups did not statistically differ with respect to age and body weight ($p = 0.07$ and $p = 0.33$, respectively). All the cats enrolled in the study were assigned an American Society of Anaesthesiologists risk classification of I. Anaesthesia was induced in all cats within 30 minutes from IM injection (Table 1). The IM

injection exceeded 1 ml volume and was therefore split into two injection sites in 10, 13 and 10 cats of groups ITL, IVM and SCL, respectively. No adverse reactions were observed.

General anaesthesia (from anaesthetic induction to active interaction) lasted 40 ± 10, 42 ± 9 and 45 ± 8 minutes in groups ITL ($n$=15), IVM ($n$=19) and SCL ($n$=15), respectively. These differences were not significant ($p$ = 0.3). The mean duration of surgery (from first incision to the last suture knot) was 8 ± 2 minutes. Physiological variables stayed within acceptable ranges for the species (Table 2), however group IVM had the lowest intraoperative respiratory rates ($p$ = 0.0009, Table 2). No statistically significant differences were found between groups and time points for HR ($p$ = 0.10 and $p$ = 0.06, respectively) and MAP ($p$ = 0.42 and $p$ = 0.82, respectively). The $SpO_2$ fell below 94% in 4 out of 49 cases, 2 of which were enrolled in group ITL and 2 in group IVM. These cats received oxygen supplementation by mask. None of the animals required endotracheal intubation (Table 2).

Intraoperatively, groups ITL, IVM and SCL received 0 (0–1), 0(0–3) and 0 (0–3) doses of propofol and 0 (0–0), 0 (0–0) and 0 (0–1) doses of fentanyl, respectively. These differences were not statistically significant ($p$ = 0.38 for propofol and $p$ = 0.86 for fentanyl, respectively). Two cats of group ITL and 3 of group SCL received intraoperative propofol, while one animal only, enrolled in group SCL, required rescue fentanyl.

Recovery was smooth and uneventful for all cats and time from atipamezole injection to recovery was shorter in group SCL [4 (3–9) minutes] than in group IVM [8 (2–17) minutes; z = 2.4], and was 6 (3–95) minutes in group ITL. Time to active interaction was 16 ± 9, 19 ± 4, and 18 ± 6 minutes in groups ITL, IVM and SCL, respectively ($p$ = 0.86) (Table 1). Postoperative SDS score was 1 (0–2) in all groups and no statistically significant difference was detected between treatments ($p$ = 0.7) (Table 3).

With respect to the postoperative pain scores performed repeatedly at four time points, no differences in UNESP-Botucatu MCPS were detected between groups ($p$ = 0.21). However,

groups SCL and ITL showed higher VAS scores than group IVM, although this difference was statistically significant only for group ITL ($p = 0.001$; Table 3).

Regarding the differences between time points, the values recorded during the first post-operative pain assessment (T5: active interaction) were the highest for both the VAS and the UNESP-Botucatu MCPS ($p = 0.008$ and $p = 0.004$, respectively). All the pain scores decreased over time (Table 3). Eight cats, four of which enrolled in group ITL, three enrolled in group SCL, and one of group IVM, received rescue buprenorphine before the completion of pain assessments. This difference was not statistically significant ($p = 0.25$).

**Discussion**

The main finding of this study is that the administration of systemic methadone, sacrococcygeal epidural lidocaine and intratesticular lidocaine resulted in comparable propofol requirements and intraoperative analgesia in male cats undergoing castration.

Our results are in agreement with those previously obtained by other authors, who found that intratesticular lidocaine injection prior to castration decreased intraoperative response to noxious stimuli in dogs (Huuskonen et al. 2012) and in cats (Moldal et al. 2013). Portier and colleagues (2009) reported similar results in horses. In the current study, intratesticular injection did not result in adverse effects and could be easily and quickly performed without requiring high level of expertise in locoregional anaesthesia. Conversely, a sacrococcygeal epidural caused relaxation of the tail and of the anal sphincter, which could be regarded as an undesirable side effect, and was technically more challenging than intratesticular injection. Moreover, the failure rate of epidural anaesthesia was found to be 9% in cats (Troncy et al. 2002), and complications and undesired effects, namely development of abscesses at the site of injection or systemic absorption of drugs, have been reported in this species (O'Hearn et al. 2011). Although cats with epidural lidocaine had intraoperative analgesia, it is unknown whether the epidural at the volume and dosages used would also result in desensitization of

the nerves in the spermatic cord. These drawbacks, together with the concern that the time required for sacrococcyegal epidural injection may even exceed the duration of such a short surgical procedure, may prevent practitioners from performing it for routine feline castration. Whilst all the three analgesic treatments seemed to provide antinociception of sufficient duration to cover the intraoperative period, the cats enrolled in the groups treated with locoregional anaesthesia had higher postoperative pain scores and also required postoperative rescue buprenorphine earlier than the cats which received methadone.

Cats in the methadone group took a longer time to recover after atipamezole administration although this did not affect the quality of the recovery. This may be attributed to enhanced and prolonged sedative effects of dexmedetomidine when the latter is combined with methadone (Menegheti et al. 2014).

The dexmedetomidine-alfaxalone combination was suitable for IM administration and resulted in reliable induction and maintenance of anaesthesia in the majority of cats. However, although the doses used in the trial had been established based on a preliminary investigation, five cats needed additional propofol to maintain unconsciousness during surgery. This may be explained by inter-individual pharmacokinetic variability, and possibly also by small variations, between cats, in the site of injection, within the fascia or in the lumbodorsal muscles.

Alfaxalone is registered for IM use in cats in Australia but not in Europe. Potential concerns for IM alfaxalone administration in feline patients are the less predictable anaesthetic effects compared to the IV route and pain upon injection, when large volumes are administered. In the cats enrolled in this study induction of anaesthesia was achieved after IM injection. However, in most of the cases the volumes exceeded one mL and had to be split into two injection sites. Large IM injections volumes are impractical and can increase the stress of the patient related to handling and restraint.

In this study the treatment groups were not composed of the same number of animals. The reason for this was that a simple randomization technique was used instead of block randomization, which would have allowed a more even distribution of the cats within groups.

In order to emulate protocols used in first-opinion veterinary practices in France, which perform more elective castrations than teaching hospitals, it was decided not to supplement inspired oxygen unless specifically needed.

The combination of dexmedetomidine and alfaxalone, with or without the addition of methadone, did not result in an appreciable decrease in respiratory rate and less than 10% of the cats enrolled in the study required oxygen supplementation. Additionally, although bradycardia did occur in some cases, the heart rate always stayed above 100 beats minute$^{-1}$; hence, according to the study protocol, none of the cats needed atipamezole administration. These results seem to indicate that the anaesthetic protocol used in this study does not causes dramatic changes in commonly monitored cardiorespiratory variables.

This study has some limitations. Junior clinicians performed the surgeries and this considerably increased the duration of the procedures compared to private practice, where experienced operators routinely perform feline castration. This might have increased the intra-operative propofol requirement, which in turn may have affected the assessment of both intra-operative nociception and post-operative pain, by influencing the cardiovascular and respiratory response during surgery and by decreasing the responsiveness to stimulation in the early postoperative period, respectively.

In conclusion, both intratesticular and sacrococcygeal epidural injections of lidocaine could be proposed as alternatives to systemic methadone to provide intraoperative analgesia in cats undergoing castration. If the duration of surgery is prolonged, the administration of additional rescue analgesics may be necessary in the early postoperative period.

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**Authors' contributions**

RF-P: performed data collection and management, interpretation of the data and preparation of the manuscript; LZ: study design, data interpretation and revised the manuscript; CF: performed data collection and management; CA: study design, statistical analysis, interpretation of data and revision of the manuscript.

## References

Adami C, Imboden T, Giovannini AE et al. (2015) Combinations of dexmedetomidine and alfaxalone with butorphanol in cats: application of an innovative stepwise optimisation method to identify optimal clinical doses for intramuscular anaesthesia. J Feline Med Surg 18, 846-853.

Brodbelt DC, Pfeiffer DU, Young LE et al. (2007) Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into perioperative small animal fatalities (CEPSAF). Br J Anaesth 99, 617-623.

Brondani JT, Mama KR, Luna SP et al. (2013) Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. BMC Vet Res 9, 143.

Haga HA, Ranheim B (2006a) Local anaesthesia for pigs subject to castration. Acta Veterinaria Scandinavica 48, (Supp l1): S13.

Haga HA, Lykkjen S, Revold T et al. (2006b) Effect of intratesticular injection of lidocaine on cardiovascular responses to castration in isoflurane-anesthetized stallions. Am J Vet Res 67, 403-408.

Hugonnard M, Leblond A, Keroack S et al. (2004) Attitudes and concerns of French veterinarians towards pain and analgesia in dogs and cats. Vet Anaesth Analg 31, 154-163.

Huuskonen V, Hughes JML, Estaca Bañon E et al. (2012) Intratesticular lidocaine reduces the response to surgical castration in dogs. Published on line in Vet Anaesth Analg 40, 74-82.

345 Jensen MP, Chen C, Brugger AM (2003) Interpretation of visual analog scale ratings
346 and change scores: a reanalysis of two clinical trials of postoperative pain. J Pain 4,
347 407-414.

348 Kamal K, Zini A, Jarvi K (2002) Testicular block using intra-testicular lidocaine: a new
349 anaesthetic technique for percutaneous testis biopsy. Can J Urol 9, 156-157.

350 Menegheti TM, Wagatsuma JT, Pacheco AD et al. (2014) Electrocardiographic
351 evaluation and degree of sedation with three doses of methadone in healthy dogs.
352 Vet Anaesth Analg 41, 97-104.

353 Moldal ER, Eriksen T, Kirpensteijn J et al. (2013) Intratesticular and subcutaneous
354 lidocaine alters the intraoperative haemodynamic responses and heart rate
355 variability in male cats undergoing castration. Vet Anaesth Analg 40, 63-73.

356 Nickell J, Barter LS, Dechant JE (2015) Effects of intratesticular and incisional local
357 anesthetic administration for castration of alpacas anesthetized with intramuscular
358 ketamine-xylazine-butorphanol. Vet Surg 44, 168-173.

359 O'Hearn AK, Wright BD (2011) Coccygeal epidural with local anesthetic for
360 catheterization and pain management in the treatment of feline urethral obstruction.
361 J Vet Emerg Crit Care 21, 50-51.

362 Portier KG, Jaillardon L, Leece EA et al. (2009) Castration of horses under total
363 intravenous anaesthesia: analgesic effects of lidocaine. Vet Anaesth Analg 36, 173-
364 179.

Troncy E, Junot S, Keroack S, et al. (2002) 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 221, 666–671.

Figure Legend

**Figure 1** Time table for intra- and postoperative assessments. Intraoperatively, cardio-respiratory variables were used to assess nociception and recorded at T0 (before surgical stimulation), T1 (after the first incision), T2 (after traction of the first testicle), T3 (after the second incision) and T4 (after traction of the second testicle). Quality of recovery was evaluated with a simple descriptive scale (SDS) as soon as the cats regained sternal recumbency. Postoperative pain assessments were carried out with a visual analogue scale (VAS) and a multidimensional composite pain scale (MCPS), as soon as the cats showed active interaction (T5) and then one (T6), two (T7) and three (T8) hours after that.

379 **Table 1** Timing data from 49 cats anaesthetized with a combination of intramuscular

380 dexmedetomidine and alfaxalone and undergoing elective castration.

| Timing | Group | | |
|---|---|---|---|
| | SLC | ITL | IVM |
| Injection to sternal recumbency (minutes) | 2 ± 1 | 2 ± 1 | 2 ± 2 |
| Injection to lateral recumbency (minutes) | 3 ± 1 | 4 ± 2 | 4 ± 3 |
| Time from injection to anaesthetic induction (minutes) | 24 ± 7 | 21 ± 9 | 19 ± 7 |
| Surgery time (minutes) | 8 ± 2 | 8 ± 2 | 8 ± 3 |
| Time from injection to atipamezole (minutes) | 40 ± 10 | 42 ± 8 | 44 ± 7 |

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384 SCL, sacrococcygeal lidocaine (*n* = 15); ITL, intratesticular lidocaine (*n* = 15); IVM,

385 intravenous methadone (*n* = 19)

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**Table 2** Mean ± standard deviation of heart rates (HR), respiratory rates ($f_R$), mean arterial pressure (MAP) and haemoglobin oxygen saturation ($SpO_2$) values of 49 cats undergoing elective castration and administered three different types of intraoperative analgesia. Measurements were taken during preanaesthetic physical examination and at five different time points: T0 (after induction of anaesthesia and before surgical stimulation, baseline), T1 (after first skin incision), T2 (after exteriorization of the first testicle), T3 (after second skin incision), and T4 (after exteriorization of the second testicle).

| Variable | Group | Time | | | | | |
|---|---|---|---|---|---|---|---|
| | | Pre-anaesthetic physical examination | T0 Baseline | T1 | T2 | T3 | T4 |
| HR (beats minute$^{-1}$) | SCL | 184 ± 21 | 119 ± 7 | 116 ± 7 | 127 ± 7 | 124 ± 7 | 136 ± 7 |
| | ITL | 188 ± 23 | 109 ± 7 | 114 ± 7 | 111 ± 7 | 103 ± 7 | 109 ± 7 |
| | IVM | 176 ± 23 | 120 ± 6 | 115 ± 6 | 122 ± 6 | 113 ± 6 | 120 ± 6 |
| $f_R$ (breaths minute$^{-1}$) | SCL | 64 ± 17 | 42 ± 2 | 41 ± 2 | 43 ± 2 | 41 ± 2 | 42 ± 2 |
| | ITL | 79 ± 19 | 42 ± 2 | 44 ± 2 | 42 ± 2 | 41 ± 2 | 42 ± 2 |
| | IVM | 77 ± 26 | 40 ± 2* | 39 ± 2* | 38 ± 2* | 34 ± 2* | 37 ± 2* |
| MAP (mmHg) | SCL | N/A | 93 ± 4 | 91 ± 4 | 89 ± 4 | 91 ± 4 | 87 ± 4 |
| | ITL | N/A | 87 ± 4 | 83 ± 4 | 90 ± 4 | 85 ± 4 | 88 ± 4 |
| | IVM | N/A | 86 ± 3 | 91 ± 4 | 92 ± 3 | 88 ± 4 | 84 ± 4 |
| SpO2 (%) | SCL | N/A | 96 ± 3 | 95 ± 3 | 96 ± 3 | 96 ± 2 | 96 ± 4 |
| | ITL | N/A | 94 ± 4 | 95 ± 5 | 94 ± 5 | 94 ± 5 | 94 ± 5 |
| | IVM | N/A | 91 ± 3 | 90 ± 4 | 90 ± 5 | 91 ± 5 | 93 ± 2 |

*Statistically significant difference between groups ($p$ = 0.009). N/A: non-applicable.

SCL, sacrococcygeal lidocaine ($n$ = 15); ITL, intratesticular lidocaine ($n$ = 15); IVM, intravenous methadone ($n$ = 19)

**Table 3** Median (range) of quality of recovery scores [assessed with a simple descriptive scale (SDS)] and postoperative pain [assessed with a Visual Analogue Scale (VAS) and with the UNESP-Botucatu multidimensional composite pain scale (MCPS)], recorded from 49 cats undergoing elective castration. Pain assessments were carried out at various time points: as soon as the cats were observed to interact actively with the investigator (T5), and then 1 (T6), 2 (T7) and 3 (T8) hours after that. SCL, sacrococcygeal lidocaine (*n* = 15); ITL, intratesticular lidocaine (*n* = 15); IVM, intravenous methadone (*n* = 19).

| Group | SDS | VAS T5 | VAS T6 | VAS T7 | VAS T8 | MCPS T5 | MCPS T6 | MCPS T7 | MCPS T8 |
|---|---|---|---|---|---|---|---|---|---|
| SLC | 1 (0-2) | 20 (0-40) | 20 (0-40) | 20 (0-20) | 20 (0-20) | 3 (0-6) | 3 (0-4) | 1 (0-4) | 1 (0-3) |
| ITL | 1 (0-2) | 20 (0-80)* | 1 (0-60)* | 1 (0-60)* | 1 (0-30)* | 2 (0-10) | 3 (0-8) | 3 (0-6) | 3 (0-5) |
| IVM | 1 (0-2) | 20 (0-20) | 20 (0-20) | 20 (0-20) | 20 (0-20) | 2 (0-6) | 3 (0-5) | 3 (1-5) | 3 (0-5) |

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406 *Statistically significant difference between ITL and IVM group ($p$ = 0.001).

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