Original Article

Analgesic Effects of Acupuncture Compared to Tramadol and Meloxicam in Cats Undergoing Ovariohysterectomy

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ABSTRACT

Background: Acupuncture has analgesic effects in animals. Common analgesics, such as opioids and anti-inflammatory drugs, are widely used to control postoperative pain in cats, but they can cause serious side effects. On the other hand, acupuncture can play a crucial role in replacing this kind of drug.

Objectives: This study aims to evaluate the analgesic effects of acupuncture compared to tramadol and meloxicam on postoperative pain in cats after ovariohysterectomy.

Methods: Forty-five adult stray cats were randomly distributed into three groups of fifteen animals each: TR: Tramadol (2 mg/kg IV) administered before anesthesia induction; ML: Meloxicam (0.2 mg/kg SC) administered after placement of the last skin suture; AC: Bilateral acupoints from kidney 11 (KI-11) to kidney 17 (KI-17) were stimulated. Postoperative pain was evaluated using the revised Glasgow composite pain scale-Feline and UNESP-Botucatu multidimensional composite pain scale (MCPS) up to 24 h after surgery. Rescue analgesia was provided intramuscularly with tramadol (2 mg/kg). Data were analyzed using the Kruskal-Wallis, Fisher's exact probability test, and Friedman test. P<0.05 is considered significant.

Results: Mean pain scores did not significantly differ among groups at any time point (P>0.05). The pain score and prevalence of rescue analgesia did not differ from the treatment groups over 24 h.

Conclusion: Based on this study, analgesic effects of acupuncture were like tramadol and meloxicam during the first 24 h after Ovariohysterectomy in cats.

Keywords: Acute pain, analgesia, Complementary medicine, Feline, Surgery

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Introduction

It has been shown that Ovariohysterectomy causes postoperative pain in cats (Lascelles BD, 1999). Common analgesic drugs, such as opioids and nonsteroidal anti-inflammatory drugs (NSAIDS), have adverse effects on dogs (Akhtardanesh et al., 2014). They can be hepatotoxic in cats or cause bradycardia, respiratory depression, gastro-intestinal (GI) toxicity, dysphoria, vomiting, and nausea (Bortolami & Love, 2015; Epstein et al., 2015).

Considering the complications of using analgesic drugs in cats, nonpharmacological modalities such as acupuncture offer a compelling pain management method for feline patients. Acupuncture is a safe, low-cost technique. It has been successfully used in companion animals to decrease pain and is now an accepted treatment modality for painful animals (Epstein et al., 2015; Lindley & Cummings, 2006).

The underlying scientific mechanisms of acupuncture and its use in modern medicine have progressed significantly. Acupuncture has evolved over centuries in both Eastern and Western cultures to become a scientifically driven and medically appropriate therapy for human and veterinary patients (Kendell, 2002). Stimulation of acupuncture points (acupoints) produces analgesia and can be achieved using various techniques, such as dry needles, electroacupuncture, aqua-acupuncture, and laser acupuncture. Dry needles, the most commonly used technique in veterinary acupuncture, involve the insertion of fine, sterile needles into acupoints (Roynard et al., 2018). After the insertion of the needle into the skin and underlying tissues, acupuncture was initiated. Acupoints are usually associated with major nerves, blood vessels, or lymphatic vessels. The acupuncture needle interacts with these structures to affect tissues near the insertion site and commences its interaction with the nervous system and distant sites (Fry et al., 2014).

According to Western acupuncture theories, stimulation of acupoints activates larger diameter fibers in the nervous system, modifies pain perception in the spinal cord, and decreases the perception of pain in the brain (Kotani et al., 2001).

Pain recognition, assessment, and quantification in animals can only be measured indirectly (Khodabakhshi Rad et al., 2023) because pain is a subjective experience, while animals are nonverbal and cannot self-report the presence of pain. It is now accepted that the most accurate method for evaluating pain in dogs and cats is not based on physiological parameters but on observations of behavioral changes (Epstein et al., 2015; Reid et al., 2018). An animal experiencing pain will try to withdraw from the source of the insult, protect the affected area through immobilization and active defensive aggression, and communicate the pain to others through changes in facial expression, body postures, and vocalization. In contrast, healthy and happy animals are identifiable by an open and relaxed posture, facial expressions of contentment, and the production of chemicals associated with pleasure, such as endorphins (Reid et al., 2018; Mc-Gowen & Goff, 2016).

The pivotal part of effective pain management is the use of a reliable, valid (being able to measure what it was designed to measure), responsive (enough sensitivity to detect health status differences that are clinically crucial), and sensible (cut-off point and responsiveness identification) pain assessment tool (Reid et al., 2007). A few pain scales have been exclusively designed for cats. In 2011, the UNESP-Botucatu multidimensional composite pain scale (MCPS) was validated for assessing acute postoperative pain in cats by Brondani et al. (Brondani et al., 2011; Buisman et al., 2017; Belli et al., 2021). A systematic review showed that the MCPS is the only pain scale that has been investigated for its validity, reliability, and sensibility in cats (Merola & Mills, 2016). The other available scale for cats is the Glasgow composite measure pain scale (CMPS), which was the first tool in veterinary medicine designed using psychometric principles, and was first used to assess acute pain in dogs (Reid et al., 2007). The latest feline version of Glasgow feline composite measure pain scale (rCMPS-F), embedded a three-point facial scale within the cat tool and provided a new validated scale for the measurement of acute pain in cats (Corletto, 2017; Holden et al., 2014).

Few studies have investigated the postoperative analgesic effects of electroacupuncture, laser, and scalp acupuncture in cats (Nascimento et al., 2019; Ribeiro et al., 2017). However, no published study has assessed the effects of acupuncture on preoperative pain management in cats.

This study evaluated the analgesic effects of acupuncture and compared these effects with those of meloxicam and tramadol in stray cats undergoing Ovariohysterectomy, using two validated feline pain scales. We hypothesized that the prevalence of rescue analgesia and pain scores would have no significant difference in the acupuncture group (AC) when compared with the meloxicam (ML) or tramadol (TR) groups.

Material and Methods

Study design and animals

Fifty-two mixed-breed stray cats were selected to participate in this study. The exact age of most cats was unknown, although all were suspected to be between 1-3 years of age. All cats were between 3-4.5 kg of weight. The health status of all cats was evaluated by physical examination and measurement of complete blood counts and total protein. All the cats were evaluated preoperatively using abdominal ultrasonography to confirm the absence of pregnancy. The exclusion criteria included the presence of systemic diseases, pregnancy, and lactation.

All cats were housed in comfortable individual cages in a calm and quiet exclusive feline ward with food and water provided ad libitum for four days before surgery. This period was used for acclimatization to the new environment.

Study design

The cats were randomly assigned to one of three treatment groups.

- TR (n=15, 2 mg kg-1 Tramadol, slow IV, immediately before induction)

- ME (n=15, 0.2 mg kg-1 Meloxicam, SQ, after placement of the last skin suture)

- AC (n=15, needles inserted from the onset of induction and remained in place for 25 minutes).

Anesthesia and surgery

Baseline (preoperative) rCMPS-F and MCPS scores were recorded 2 hours before sedation. Cats were premedicated with ketamine hydrochloride [ketamine 10%; Alfasan Woerden-Holland, 3 mg/kg IM)]. Approximately 20-10 minutes after sedation, ketamine hydrochloride (5 mg/kg, IV) and diazepam (Zepadic; Caspian Tamin, 0.05 mg/kg, IV) were administered to allow endotracheal intubation. Isoflurane (Forane; Abbott Laboratories) was administered using a non-rebreathing circuit to maintain anesthesia. Ovariohysterectomy was performed by the same surgeon using a 3 cm ventral midline approach and three clamp technique through median laparotomy access (MacPhail & Fossum, 2018).

Anesthesia time (time from induction of anesthesia to discontinuation of isoflurane), surgery time (time from the first incision until placement of the last skin suture), and time to extubation (time from termination of isoflurane until extubation) were recorded for each cat (Table 1).

Acupuncture treatment

The acupuncture needles were administered after induction of anesthesia and remained in place for 25 minutes. Local acupoints on the stomach meridian from kidney 11 (KI-11) to KI-17 were stimulated bilaterally. The exact location of each acupuncture point was determined by the traditional Chinese principles, using the "cun" measurements (1 cun=width of the last rib) (Marten, 2012)

- KI-11: On the cranial edge of the pelvic symphysis, about 0.5 cun lateral to CV-2

- KI-12: 1 cun each cranial to KI-11 and lateral to CV-3

- KI-13: 1 cun lateral to CV-4, one cun lateral to the midline halfway between the navel and pelvic symphysis.

- KI-14: 2 cun caudal to the navel, one cun lateral to the CV-5.

- KI-15: 1 cun lateral to CV-7 and one cun from the midline.

- KI-16: 1 cun lateral to CV-8 and one cun lateral to the midline next to the navel.

- KI-17: 1 cun lateral to CV-10.

Sterile stainless-steel needles (Dong Bang Acupuncture, Seoul, South Korea, size 0.18×13 mm) were inserted tangentially to a depth of 0.2-0.3 cun and kept for 25 minutes.

Postoperative assessments

Cats were returned to their cages, and the pain scores were evaluated by the same single observer, unaware of the treatment groups 2, 4, 7, 13, and 24 h after tracheal tube extubation.

Cats were scored for signs of pain using the Glasgow scale (rCMPS-f, from 0=no pain to 20=maximum pain) (Reid et al., 2007) and UNESP-Botucatu scale (MCPS, from 0=no pain to 30=maximum pain) (Buisman et al., 2017).

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For scoring, each cat's behavior was initially evaluated for one minute without opening the cage. Subsequently, the cage was opened, and the cat was touched and stimulated to move around to observe reactions, interactions, and behavior. Finally, the incision and surrounding area of the abdomen were palpated using 2–3 digits.

In addition, to minimize variability between different observers and improve objectivity, all measurements in this study were performed by the same observer, blinded to the group allocation, who was caring for the cats during the study and was familiar with their behavior.

Cats scoring greater than 33% in either the rCMPS-F or MCPS maximum score received tramadol (2 mg/kg, IM) as rescue analgesia. The pain score was evaluated 30 minutes after rescue analgesia (Holden et al., 2014).

The number of cats requiring rescue analgesia was recorded. Data collected after rescue analgesic administration were not included in the statistical analysis.

Statistical analysis

Pain scores were analyzed using the Kruskal-Wallis test to compare differences between treatment groups at each time point, and the Friedman test was used to compare differences over time for each treatment group.

The Friedman test was also used to compare differences in pain scores over time within each group. Corresponding areas under the curves of rCMPS-F and MCPS were calculated from baseline to 24 h using the trapezoidal method and compared among groups using the Kruskal–Wallis test. Data on pain scores obtained after the first rescue analgesia dose were removed from the analyses.

The number of cats that required rescue analgesia was compared using the Fisher exact probability test.

Statistical analyses were performed using the SAS software, version 9.4 (Proc Univariate & Proc ANOVA, SAS version 9.0; SAS Institute Inc., Cary, NC, USA).

Results

Fifty-two cats were screened for enrollment in the study. Seven of these did not meet the inclusion criteria (three had signs of systemic disease, and four were in the early stages of pregnancy).

Table 1 presents the duration of anesthesia and surgery, time to extubation, and body weight. These variables were not significantly different among treatment groups (P>0.05). None of the cats showed postoperative complications or adverse effects.

Mean MCPS and rCMPS-F pain scores did not significantly differ among groups at any time point (P>0.05) (Figure 1 and 2).

Compared with baseline values, MCPS pain scores were significantly higher in the first 7 h after extubation in all treatment groups (Table 2). rMCPS-F pain scores were significantly higher than baseline 4 and 7 h after surgery in all treatment groups (Table 2).
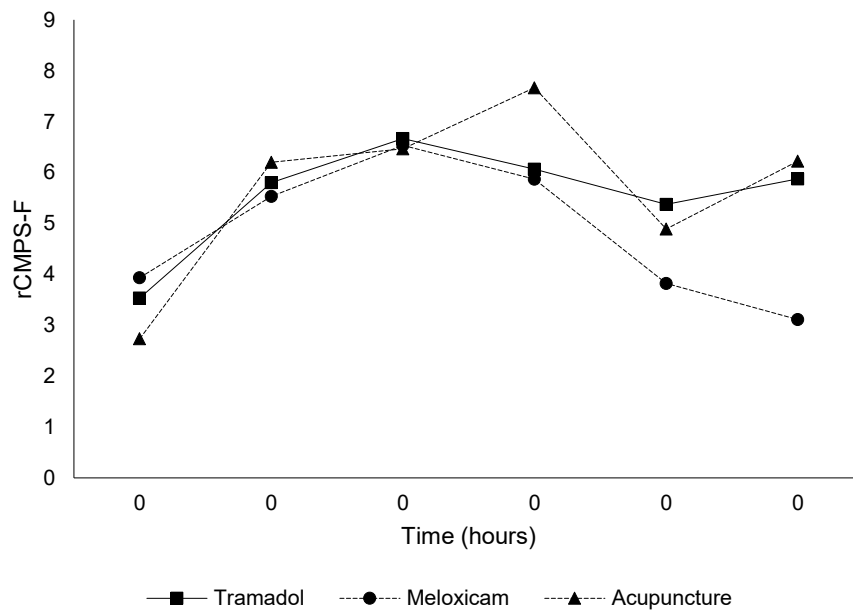
Repeated measures analysis results showed that the difference between the two pain measurement scales was not significant after 24 h; however, rCMPS-F had significantly lower scores compared to MCPS at 2 and 4 h after extubation, and the difference decreased at 7, 13, and 24 h after extubation. Hence, the two methods were the same in measuring the pain in a 24-h basis (Figure 3).

On the other hand, comparing the two scales in each treatment group using the Friedman test showed that in the tramadol group, MCPS evaluated pain significantly higher than rCMPS-F at 2 and 4 h after extubation.

Table 1. Body weight, anesthesia and surgery times, and time to extubation in treated cats

Variables	Mean±SD		
	TR (n=15)	ML (n=15)	AC (n=15)
Weight	3.5±0.45	3.43±0.49	3.28±0.55
Anaesthesia time	58.3±13.8	56.8±12	55.5±13.8
Surgery time	45.2±11.4	46.5±10.8	42±7.9
Time to extubation	14.5±9.1	14±5.2	15.8±4.4

Abbreviations: TR: Tramadol; ML: Meloxicam; AC: Acupuncture.

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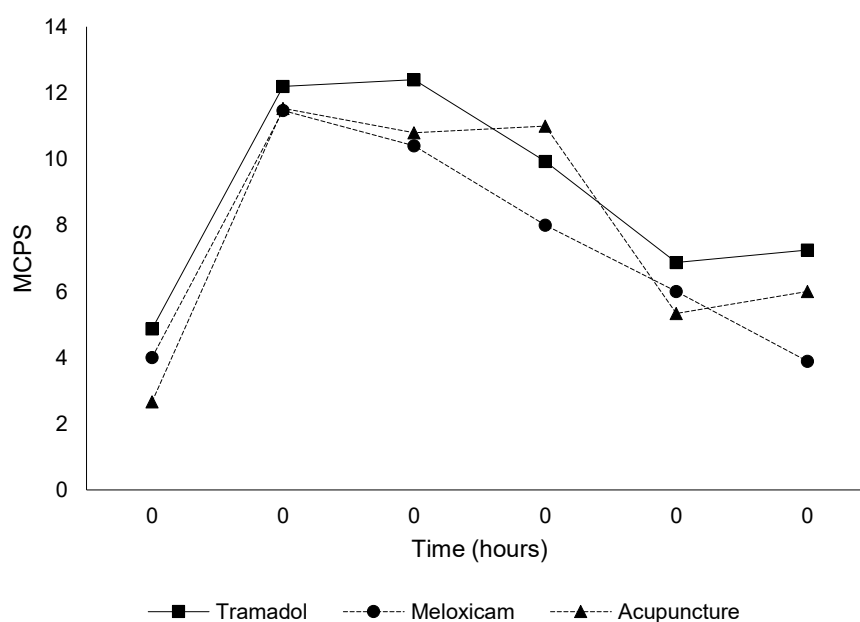
Figure 1. Mean±SD pain score based on rMCPS-F, 2 h before and 2-24 h after surgery

In meloxicam group, MCPS method evaluated the pain significantly higher only in 2 h after extubation. The same is true about the acupuncture group, where the MCPS method evaluated the pain significantly higher 2 h after extubation; however, in this group, MCPS evaluated the pain significantly lower than rCMPS-F in 24 hours after extubation.

Twenty cats required rescue analgesia. The number of cats that required rescue analgesia did not differ significantly between groups (Table 3). The time to first rescue analgesia did not differ among the treatments (P>0.05). None of the cat required a second dose of rescue analgesia.

The results of this study showed that postoperative pain scores and the prevalence of rescue analgesia were not significantly different among treatments using the MCPS and rCMPS-F pain scores.

Figure 2. Mean±SD pain scores based on MCPS, 2 h before surgery and 2-24 h after surgery

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Table 2. Pain scores measured before surgery and 2, 4, 7, 13 and 24 hours after extubation in three groups

Treatment	Scale	Time (h)					
		BL	2	4	7	13	24
TR	rCMPS-F	1.5(0- 11)	5(3-11)†	6(4-11)*†	6(2-10)*	5(2-10)	3(1-12)
	MCPS	1(0-16)	12(9-16)*	12(7-20)*	9.5(0-18)*	6(0-14)	8(0-16)
ML	rCMPS-F	5(0-10)	5(3-7)†	6(3-11)*	5.5(2-11)*	3(1-9)	3(1-10)
	MCPS	3.5(0-13)	11(9-15)*	10.5(5-15)*	8.5(0-15)*	6(1-13)	2(0-13)
AC	rCMPS-F	2.5(0-7)	6(5-8)*†	6(4-12)*	8(3-11)*	7(0-7)	7(1-9)*
	MCPS	1(0-10)	12(9-14)	11(9-13)*	10.5(8-19)*	4(1-11)	6(1-9)*†

Abbreviations: BL: Before surgery; TR: Tramadol; ML: Meloxicam; AC: Acupuncture.

*Significant difference compared to baseline (P<0.05); †Significant difference between to two scales (P<0.05).

Discussion

In this study, the analgesic effect of acupuncture was evaluated and compared to that of meloxicam and tramadol. The latter two treatments are often used in the management of postoperative pain in cats, and there are currently concerns about their use in feline practice because they can cause mild to serious adverse effects, including bradycardia, respiratory depression, GI toxicity and nephrotoxicity (Epstein et al., 2015).

In recent years, evidence-based data and empirical experience have justified the use of acupuncture in small-animal practice (Epstein et al., 2015; Roynard et al., 2018; Cassu et al., 2012). Acupuncture is a safe method in veterinary patients and can provide analgesia comparable to that achieved with injectable opioids or NSAIDS (Fry et al., 2014).

The results of this study demonstrated that postoperative pain scores and the prevalence of rescue analgesia were not significantly different among treatments using both rCMPS-F and MCPS, confirming the hypothesis of this study. These results are supported by clinical reports, where perioperative acupuncture caused effective analgesia compared to conventional analgesic drugs and reduced the need for supplemental analgesics in small animals (Nascimento et al., 2019; Ribeiro et al., 2017; Gakiya et al., 2011).
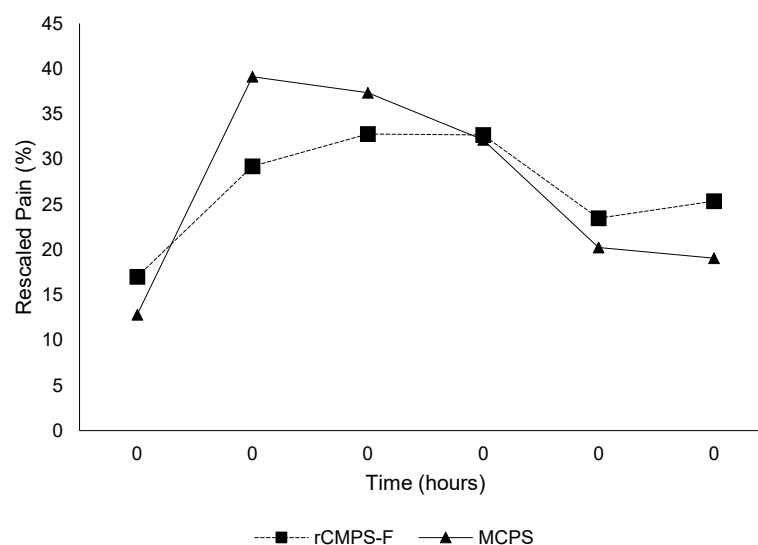
Figure 3. Mean±SD of pain scores for three treatment groups based on homogenized MCPS and rCMPS-F 2 h before surgery and 2-24 h after surgery

Notes: Asterisks show significant differences at an alpha level of 0.05.

Table 3. Number of cats that received rescue analgesia based on rCMPS-F and MCPS (scores ≥33% of maximum score) following ovariohysterectomy.

Group	Time (h)		4	7	13	24	Total
	BL	2					
TR	0	0	0	7	0	0	7
ML	0	0	0	4	2	0	6
AC	0	0	0	6	0	1	7

Abbreviations: BL: Before surgery; TR: Tramadol; ML: Meloxicam; AC: Acupuncture.

This study used two scoring systems (rCMPS-f and MCPS) to obtain a more reliable impression of pain. Both scales have been used to measure pain following Ovariohysterectomy in cats (Merola & Mills, 2016; Nascimento et al., 2019; Steagall et al., 2018). Other studies also failed to show significant differences in pain scores between groups when the rCMPS-f or MCPS scale was used in cats (Teixeira et al., 2020; Steagall et al., 2018; Marques et al., 2015). This can be explained by several limitations.

Cats that received rescue analgesia were removed from the statistical analysis to avoid analysis bias while simultaneously introducing a selection bias. This approach limited the ability to detect significant differences among treatments using pain scores. However, the scores were increased in all treatment groups at 2 h, 4 h, and 7 h using the MCPS and at 7 h using the rCMPS-F when compared with baseline values. This reflects that pain scores are commonly higher after surgery than baseline values.

Given the subjectivity of pain and scoring systems, observer training and familiarity with the cats' normal behavior are pivotal to identifying pain (Reid et al., 2018; Benito et al., 2017). In the current study, pain was assessed by a veterinary student who received video-based training in feline pain assessment. While the observer spent a week with the cats to familiarize themselves with their individual behavior and responses, it is possible that lack of experience played a role in the results.

Small sample size and absence of a negative control group. Having a negative control group made it easier to detect subtle treatment effects; however, a negative control group was not included for ethical reasons. Also, this study did not include a placebo acupuncture group. It has been shown that placebo acupuncture (non-acupuncture points stimulated by needles) may also produce an analgesic response, although more potent effects are achieved by real point stimulation (Chen et al., 2016).

The stimulation of sham points reduced the pain threshold in dogs, rats, and rabbits; however, the stimulation of real points provided a more intense response (Kotani et al., 2001; Cassu et al., 2008) Due to the low analgesic effects reported with sham point stimulation, the decision made not to include a placebo acupuncture group in the study.

Both MCPS and rCMPS-f recorded statistically similar pain over the 24-h period. However, the rCMPS-F had significantly lower scores than the MCPS at 2 and 4 h after extubation. Many of the items in the rCMPS-F are similar to UNESP-Botucatu MCPS, including behavioural categories-vocalization, posture, attention to wound, response to people, response to touch, and demeanor (Merola & Mills, 2016). Other similarities between the rCMPS-F and the UNESP-Botucatu scale include the ranking of the items within each category according to the pain intensity and the provision of a protocol that ensures consistency of the assessment procedure (Brondani et al., 2011; Buisman et al., 2017). Thus, the rCMPS-F has good overlap and is common with MCPS in general use. However, in contrast to rCMPS for cats, which considered a variety of procedures, UNESP-Botucatu only considered Ovariohysterectomy as a pain mode for its validation; thus, it is a more reliable tool for measuring acute pain after OHE.

Buisman et al. showed that the use of anesthetic protocols that affect behavior can be a confounding factor in the assessment of pain using MCPS in the early postoperative period (Buisman et al., 2015). Previous studies reported that ketamine might induce behavioral changes during recovery from general anesthesia, including ataxia, hyperreflexia, hypersensitivity to touch and noise, and increased motor activity (Gieseg et al., 2014) One study showed that the mean time for cats to recover normal behavior following ketamine (3 mg/kg) in combination with midazolam (0.5 mg/kg) was 4.28±3.12 h (Ilkiw et al., 2002). A recent study demonstrated that the admin-

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istration of ketamine (5 mg/kg) before general anesthesia with isoflurane in cats produced psychomotor changes, increasing in scores evaluated by MCPS until the third hour of assessment (Buisman et al., 2015).

Also, pretreatment with ketamine and diazepam can interfere with the analgesic response to acupuncture (Xu et al., 1989). Studies support a similar clinical effect in dogs, although ketamine's analgesic effect has not yet been studied in a feline surgical model (Slingsby & Waterman-Pearson, 2000; Wagner et al., 2002). In addition, benzodiazepines potentiate GABAergic activity, which could interfere with the acupuncture effects since the GABAergic system is also involved in the analgesic pathways of acupuncture (Qiao et al., 2017). Currently, there is no published data on the analgesic effects of acupuncture in cats pretreated with ketamine and diazepam. Several studies have investigated the effects of ketamine and benzodiazepines on acupuncture-induced analgesia. The results of studies on laboratory animals indicated that ketamine may have an antagonistic effect on acupuncture analgesia (Xu et al., 1989).

Tramadol can produce adverse behavior responses in cats, including excitation, euphoria, and panting. No adverse effects were observed in the current study. In addition, no local adverse effects related to acupuncture were identified, suggesting that acupuncture is a safe alternative to provide analgesia in cats. These results are supported by previous studies that reported the safety of acupuncture therapy in dogs and cats (Cassu et al., 2012; Gakiya et al., 2011; Nascimento et al., 2019).

A significant limitation of this study was that all a surgical resident performed all acupuncture treatments with a year of experience in animal acupuncture. A significant difference was observed in the accuracy of acupuncture needle placement among veterinary acupuncturists with different clinical experience. Accurate needle placement is needed for the appropriate stimulation of neural, fascial, vascular, and other structures that may be small to microscopic. Therefore, variability in needle placement can profoundly influence clinical effects (Yang et al., 2007).

In conclusion, in this study, postoperative analgesia was not significantly different between the treatment groups using both MCPS and rCMPS-f. These findings suggest that acupuncture might be a crucial alternative in the treatment of perioperative pain in cats and can be an alternative to conventional analgesics, such as NSAIDS and opioids. Larger, sham-controlled studies are required to support these results.

Ethical Considerations

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