DOI: 10.5433/1679-0359.2016v37n6p4063

Effects of epidural anesthesia with tramadol, ropivacaine or tramadol-ropivacaine combination, in bitches undergoing ovariohysterectomy under anesthesia with isoflurane

Efeitos da anestesia epidural com tramadol, ropivacaína ou sua associação, em cadelas submetidas à ovariosalpingohisterectomia sob anestesia com isoflurano

Daiane Cristina Winter[1*]; Samuel Monzem[1]; Paulo Roberto Spiller[1]; Matias Bassinello Stocco[1]; Lianna Ghisi Gomes[1]; David Ronald Parra Travagin[2]; Elaine Dione Venêga da Conceição[3]; Luciana Dambrósio Guimarães[4]

Abstract

Epidural anesthesia is a locoregional anesthetic technique that provides analgesia and muscle relaxation in the-retroumbilical region. The combination of opioids and local anesthetics increased the intensity and duration of analgesia by causing immediate motor and sensory nerve blockade, and improved recovery after surgery. The objective was to comparatively evaluate the trans- and postoperative cardiorespiratory and analgesic effects of epidurally administered tramadol, ropivacaine and tramadol-ropivacaine combination in dogs undergoing elective ovariohysterectomy. The effect of isoflurane concentration was also evaluated. This study was performed on 24 female mongrel dogs, pre-medicated with chlorpromazine (0.5 mg kg^{-1}, IV) and, anesthetized with propofol and isoflurane. The dogs were randomly divided into three groups. The first group receveid epidural tramadol (2 mg kg^{-1}, GT group), the second group received ropivacaine (1.5 mg kg^{-1}, GR group), and the third group received a tramadol-ropivacaine combination at the above-mentioned doses (GTR group). At pre-defined time points, classified into pre-, trans-, and postoperative periods, cardiorespiratory variables and analgesia were analyzed for a period of up to 420 min following epidural anesthesia. The check analgesia was check of approximately 105, 217 and 382 minutes, in GR, in GT and GTR respectively, and no cardiovascular and respiratory depression. The drugs used in this study are considered safe and effective for ovariohysterectomy due to the cardiorespiratory stability and trans-operative analgesia provided by them. However, the combination of ropivacaine and tramadol ensured a greater reduction in the inhaled anesthetic dose and better analgesia during in the postoperative period.
Key words: Analgesia. Pain. Locoregional.

Resumo

A anestesia epidural é uma técnica anestésica locorregional que proporciona analgesia e relaxamento muscular na região retroumbilical. A associação de opioides com os anestésicos locais contribui para o

[1] Discentes do Programa de Pós-Graduação em Ciências Veterinárias, Universidade Federal de Mato Grosso, UFMT, Cuiabá, MT, Brasil. E-mail: dai_winter@hotmail.com; s.monzem@hotmail.com; paulo_spiller@hotmail.com; matiasnave@hotmail.com; liannaghisi@gmail.com

[2] Prof., Especialista do Curso de Medicina Veterinária, Faculdade Integrado, Campo Mourão, PR, Brasil. E-mail: dparratravagin@gmail.com

[3] Profª Drª, Instituto de Ciências da Saúde, UFMT, Sinop, MT, Brasil. E-mail: elainedione@gmail.com

[4] Profª Drª, Programa de Pós-Graduação em Ciências Veterinárias, UFMT, Cuiabá, MT, Brasil. E-mail: luguima@bol.com.br

[*] Author for correspondence

Received: Feb. 19, 2015 - Approved: Aug. 27, 2016

aumento da intensidade e prolongamento da analgesia, ocorrendo bloqueio sensitivo e motor imediato, melhorando a recuperação no período pós-operatório. Objetivou-se avaliar comparativamente no trans- e pós-operatório, os efeitos cardiorrespiratórios e a analgesia proporcionada pelo tramadol, ropivacaína ou sua associação, pela via epidural, bem como a concentração anestésica do isoflurano no trans-operatório, em cadelas submetidas à ovariosalpingohisterectomia eletiva. Este estudo foi realizado com 24 fêmeas da espécie canina, pré-medicadas com clorpromazina (0,5 mg Kg^{-1} IV), anestesiadas com propofol (à efeito) e isoflurano, e distribuídas aleatoriamente em três grupos, nas quais foi utilizado pela via epidural 2 mg Kg^{-1} de tramadol (GT), 1,5 mg Kg^{-1} de ropivacaína (GR) ou sua associação (GTR) nas doses citadas anteriormente. Em momentos pré-definidos, dos períodos pré, trans- e pós-operatório, foram analisadas variáveis cardiorrespiratórias e a analgesia por um período de até 420 minutos após a anestesia epidural. Pode-se verificar analgesia de aproximadamente 105, 217 e 382 minutos, no GR, no GT e no GTR respectivamente, e ausência de depressão cardiovascular e respiratória. Os fármacos utilizados neste estudo podem ser considerados seguros e eficientes para a técnica cirúrgica em questão devido à estabilidade cardiorrespiratória e analgesia trans-operatória, porém, a associação de ropivacaína e tramadol promoveu maior redução no anestésico inalatório e melhor analgesia no período pós-operatório.

Palavras-chave: Analgesia. Dor. Locorregional.

Introduction

In recent decades, the use of drugs and techniques that ensure appropriate anesthesia and pain control have been the subject of intense discussion. The assessment of pain in animals is based on both the physiological parameters and the behavioral aspects, and because of their subjectivity, these assessments are difficult to perform (BRONDANI et al., 2004; PAOLOZZI et al., 2011; POHL et al., 2011; LANDA, 2012; MORGAZ et al., 2013). Physiological parameters are critical to the assessment of pain, especially during the transoperative period, and include, among other variables, heart rate (HR), respiratory rate (F), body temperature (T, ºC), and blood pressure (BP) (BRONDANI et al., 2004; LANDA, 2012). Postoperative pain is also diagnosed based on an evaluation of behavioral characteristics, using methods such as the visual analogue scale (VAS). The VAS is a line measuring 10 cm, with marks at the two ends corresponding to no pain and worst pain possible (CARREGARO et al., 2010; POHL et al., 2011; LANDA, 2012; SOUZA et al., 2013; TEIXEIRA et al., 2013). This scale is routinely used in postoperative evaluation of various surgical procedures, one of which is ovariosalpingohysterectomy (OSH) (CARREGARO et al., 2010; POHL et al., 2011; ADAMI et al., 2012; MORGAZ et al., 2013; TEIXEIRA et al., 2013).

OSH is routinely performed in veterinary medicine, mainly as a procedure for population control in animals (POHL et al., 2012). It causes mild to moderate pain during the trans- and postoperative periods (FLOWER et al., 2012; PEREZ et al., 2013). Therefore, it is of paramount importance that the anesthetic protocol and the analgesic used during surgery are effective. It is essential that they be administered in a balanced manner through a combination of techniques and drugs in order to reduce the adverse effects (TONNER, 2005; BASSO et al., 2008; TEIXEIRA et al., 2013). The premedication (MPA) often used includes phenothiazines such as chlorpromazine. Phenothiazines cause an antiemetic effect by blocking the neurotransmission of serotonin and dopamine in the central nervous system (CNS), causing sedation, muscle relaxation, and possible hypothermia. Its primary side effect is related to hypotension with reflex tachycardia. However, at low doses the effect is virtually absent (ARENA et al., 2009).

Volatile and intravenous anesthetics are widely used in veterinary medicine, prominent among which are propofol and isoflurane. These

anesthetics cause dose-dependent cardiovascular and respiratory depression (BARBOSA, 2007; BORGES et al., 2008). When combined with opioids, they reduce the adverse effects, thereby providing an improved and balanced anesthetic effect (TONNER, 2005; ADAMI et al., 2012). Epidural anesthesia is a locoregional technique used in multimodal (or balanced) anesthesia (TONNER, 2005; BASSO et al., 2008; PEREZ et al., 2013; SOUZA et al., 2013). It is capable of providing analgesia and muscle relaxation in the retroumbilical region (SOUZA et al., 2013) and causes minimal cardiorespiratory changes. It also improves control over postoperative pain, reduces transoperative stress (ALBUQUERQUE et al., 2010), is safe and efficient, and can reduce the concentration of inhaled anesthetic required for the maintenance of proper anesthesia (VALVERDE, 2008; ITAMI et al., 2011; BOSMANS et al., 2011; NATALINI et al., 2011).

The biggest disadvantages of epidural (ED) anesthesia are its localization in the retroumbilical region and its short anesthetic duration when used as a local anesthetic only (ISHIY et al., 2002). Lidocaine and bupivacaine are commonly used in veterinary medicine. Ropivacaine, a pure S enantiomer, provides significant advantages over its precursor, bupivacaine, including reduced motor nerve blockade, lower-intensity action on the fibers responsible for motor action, and lower cardiotoxicity. However, its use is limited because of its high cost (VAN DE VELDE et al., 2007; SILVA et al., 2008; ALBUQUERQUE et al., 2010; SOUZA et al., 2013). Local anesthetics, which produce sensory block and immediate engine, when combined with ED opioids, increase the duration and intensity of analgesic effect, contributing to the acceleration in the postoperative recovery of the animal (VALADÃO et al., 2002; BASSO et al., 2008).

Opioids, in turn, relieve somatic and visceral pain by blocking the nociceptive impulses without interfering with the sensory and motor functions and the functioning of the sympathetic nervous system (COUSINS; MATHER, 1984). Epidural morphine, fentanyl, methadone, and tramadol are commonly administered. Tramadol is an atypical opiate, which in addition to binding to the opioid receptors, inhibits the reuptake of norepinephrine and serotonin (GUEDES et al., 2002; BASSO et al., 2008; BORGES et al., 2008; MCMILLAN et al., 2008; SILVA et al., 2008; ITAMI et al., 2011). It also exhibits local anesthetic action by blocking the sodium channels in nociceptive C fibers and A-delta (BASSO et al., 2008; KARGI et al., 2008). Tramadol does not cause severe hypotension and histamine release (MARUCIO; COTES, 2012). It produces minimal depressant effects in the CNS and cardiorespiratory system, observed in other opioids, and features a postoperative analgesic effect for 4 to 12 hours, similar to morphine (GUEDES et al., 2002; BASSO et al., 2008; KARGI et al., 2008; MCMILLAN et al., 2008; PAOLOZZI et al., 2011).

The combination of drugs for ED anesthesia tends to result in the potentiation of anesthetic and analgesic effects, reduction in the side effects from the isolated use of drugs, as well as a reduction in the required dose and toxicity (VALADÃO et al., 2002; CASSU et al., 2008; SILVA et al., 2008; ALBUQUERQE et al., 2010; REGALIN et al., 2014). Ropivacaine when combined with an opioid analgesic is efficient, but when administered alone is not able to provide adequate analgesia during an orthopedic surgical procedure (ADAMI et al., 2012). A small volume (0.2 $ml \cdot kg^{-1}$) does not provide the suitable blocking time required for conducting OSH and therefore requires intraoperative analgesic rescue (ALBUQUERQUE et al., 2010; REGALIN et al., 2014).

Given the beneficial effects of tramadol and ropivacaine and the lack of studies evaluating the use of their combination in dogs, we aimed to compare the cardiorespiratory and analgesic effects provided by ED tramadol, ropivacaine, and the tramadol-ropivacaine combination during the trans- and postoperative periods. We also evaluated the effect

of anesthetic concentration of isoflurane during surgery in bitches undergoing ovariohysterectomy.

Material and Methods

The Ethics Committee on Animal Use (CEUA) of the Federal University of Mato Grosso (UFMT) approved this study (Nº23108.025549 protocol / 13-8). The owners authorized the participation of animals in research by signing the consent form.

The studied included 24 mongrel female dogs, with a mean age of 4 ± 2 years and average weight of 14.66 ± 8.1 kg from the routine patients at the Veterinary Hospital (HOVET) of the Federal University of Mato Grosso (UFMT), Cuiabá campus. The animals were considered clinically asymptomatic by clinical and laboratory tests (blood count, creatinine, and ALT) and classified as ASA I, being discarded or lactating female estrus.

The animals were deprived of solid food and water for at least 12 and 2 hours, respectively. They were catheterized in the cephalic vein and infused with lactated Ringer's solution (Ringer lactate 500 mL Equiplex, Goias, Brazil; 10 $ml \cdot kg^{-1} \cdot h^{-1}$) and the anesthetic drug cephalothin (sodium cephalothin, 200 $mg \cdot ml^{-1}$, ABL Brazil Antibiotics, São Paulo, Brazil; 30 $mg \cdot kg^{-1}$) 30 minutes before the start of anesthesia.

After 15 minutes of premedication (MPA) with chlorpromazine (chlorpromazine, Hypofarma, Minas Gerais, Brazil; 0.5 $mg \cdot kg^{-1}$, IV), the animals were placed under anesthesia with propofol (Propofol 10 $mg \cdot ml^{-1}$, Provive®, Meizher Biopharma S / a, São Paulo, Brazil) in dose effect, to allow intubation with a probe of an appropriate diameter. Anesthesia was maintained under spontaneous ventilation with 1.5 volume percent (v%) isoflurane (Isoforine®, 100 mL, Cristália, São Paulo, Brazil) and a diluent flow of 100% oxygen. This anesthetic system was determined to be suitable based on the animal's weight. Anesthetic concentration was reduced by 0.5% (v%) when the HB or systolic blood pressure (SBP) decreased by 20% compared to baseline.

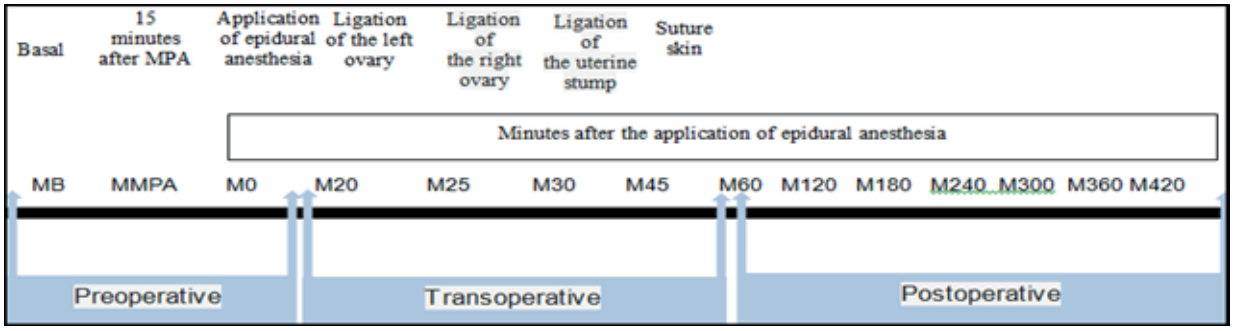
At the start of the maintenance period, the animals were randomly distributed into three groups (each n = 8). One group was administered ED tramadol (GT group; tramadol hydrochloride, 50 $mg \cdot ml^{-1}$, Teuto's, Goiás, Brazil; 2 $mg \cdot kg^{-1}$), the second group received ED ropivacaine (GR group; ropivacaine Ropi®, 7.5%, Cristália, São Paulo, Brazil; 1.5 $mg \cdot kg^{-1}$) and the third group received a combination of GT-GR (GTR group; in the above mentioned doses). Drugs were diluted in sterile injection water (water for injection, 10 ml, Isofarma, Ceará, Brazil) to a fixed final volume of 0.4 $ml \cdot kg^{-1}$ (CASSU et al., 2008), which was administered epidurally in the lumbosacral region (LS) according to the methodology described by Jones (2001). The animals were kept in sternal recumbency for five minutes and then repositioned in the supine position for the surgery, which started 15 minutes after the application of ED anesthesia.

OSH for all the groups was performed using the two-clamp technique with a pre-set time for each surgical stimulation step, ending 45 minutes after ED anesthesia. The same surgical team performed all OSH procedures. The dogs were wrapped under a thermal mattress (Ortovet®, Styllus term, São Paulo, Brazil) during surgery to maintain the body temperature within the appropriate limits.

The variables were evaluated 15 minutes after premedication (MMPA) and immediately after the ED block (M0) before the application of any medication (MB). During the transoperative and postoperative assessment, the time points for evaluation after the ED block were related to surgical stimulation as follows: M20 (20 minutes; arteriovenous complex ligation of the left ovary), M25 (25 minutes; arteriovenous complex ligature of the right ovary), M30 (30 minutes; ligation of the uterine stump), M45 (45 minutes, end of skin suture). M60, M120, M180, M240, M300, M360, and M420 correspond to evaluation at 60, 120, 180, 240, 300, 360, and 420 minutes respectively (Figure 1).

At all time points, the body temperature (T, °C) was evaluated using a rectal thermometer. The values were digitally recorded using a multiparameter monitor while the animal was anesthetized and, with a digital thermometer when it was conscious. The heart rate (HR), in beats per minute (bpm), was measured using a stethoscope. The SBP, in millimeters of mercury (mmHg), was measured in triplicate using a noninvasive oscillometer whose cuff size is equal to 1/3 the circumference of the limb. The oscillometer was positioned above the metacarpal region of the right forelimb. The respiratory rate (f), in strokes per minute (mpm), was determined by the number of thoracic excursions per minute, through direct observation of the ribcage expansion.

Figure 1. Timing chart (in min) showing the experimental design. The time points for evaluation are divided into three periods: before (Preoperative), during (Transoperative), and after (Postoperative) ovariohysterectomy under isoflurane anesthesia. The animals are divided into three groups based on the drug used for lumbosacral epidural block: tramadol group (GT), ropivacaine group (GR), and tramadol-ropivacaine combination group (GTR).



During the transoperative period, parameters were directly recorded using a multiparameter monitor. The carbon dioxide concentration at the end of exhalation ($ETCO_2$, in mmHg), was evaluated with the main flow sensor coupled between the endotracheal tube and the anesthetic system. The oxygen saturation of hemoglobin (in %), was measured using pulse oximetry (SpO_2). The transmitter / sensor adapted in the language of each animal and expired fraction of isoflurane (FEISO) was expressed in volume percentage (v%).

The blood gas analysis was performed on an arterial blood sample (0.5 ml), collected directly by puncturing the left metatarsal artery with a previously heparinized insulin syringe (Hepamax-S®, 5000 IU mL^{-1}, Blau, São Paulo, Brazil). The sample was analyzed immediately after collection. We evaluated the partial pressure of oxygen in arterial blood (PaO_2, in mmHg), partial pressure of carbon dioxide in arterial blood ($PaCO_2$, in mm Hg), oxyhemoglobin saturation in arterial blood (SpO_2, in %), and hydrogenionic potential (pH) at four different time points (M0, M25, M45, and M120).

The same observer evaluated the degree of analgesia after ED every 60 minutes for 420 minutes or until the time of rescue analgesia. The observer was unaware of the treatment used, which was based on the results from the VAS, where zero meant no pain and 10 indicated the worst pain imaginable. As mentioned earlier, the VAS scale is based on the behavior of each animal. Patients were observed prior to the administration of any drug and the behavior was compared to that demonstrated during the postoperative period. During both time periods, the behavioral evaluation of the animals was performed with and without interaction with the viewer.

In animals that showed a 20% increase in HR and SBP compared to the baseline value and an EVA graduation equal to five, analgesia was maintained with morphine rescue (Dimorf®, 10 mg ml-1, Cristalia, São Paulo, Brazil; 0.2 mg·kg^{-1} IM), and further evaluations were stopped. Meloxicam (Maxicam® 20 mg·ml^{-1}, thin gold, São Paulo, Brazil; 0.2 mg·kg^{-1}, IM) was administered after 420 min on the day of ED anesthesia or at the time of analgesic rescue. The same dose was administered for three consecutive days as postoperative analgesic (0.2 mg kg^{-1}, orally).

This study is based on a completely randomized design, using a split-plot time scheme. Data were analyzed using a one-way analysis of variance (ANOVA), followed by a Scott-Knott test. Differences were considered statistically significant at $p < 0.05$.

Results and Discussion

Table 1 shows that there the HR, SBP, and F reduced 15 minutes after application of chlorpromazine. These reductions are statistically significant only in the GR and GTR groups. According to Arena et al. (2009), hypotension and reflex tachycardia are the main side effects of phenothiazines. However, we did not observe these effects in our study, probably due to the low dose administered. The reduction in these variables observed in this study can be explained by the tranquilizing effect on F (SILVA et al., 2008).

Soon after induction (M0), a significant reduction was noted in SBP in the GTR group and in F in all the groups. These changes can be attributed to the respiratory depressant effect and cardiovascular propofol bolus (BARBOSA, 2007). The change in SBP only in the GTR was due to the higher value at baseline, which could be caused by stress (ANDRADE, 2002). Mean values after the induction varied between 135 and 140 mmHg in all groups and remained within the physiological range for the species. There were no significant differences between the groups.

During the transoperative period, there are no significant differences in T, HR, RR, $ETCO_2$, and SpO_2 between the groups and at various time points (Table 1). Similarly, there were no differences in PaO_2, $PaCO_2$, $SatO_2$, and pH (Table 2). Table 1 shows a statistically significant difference in SBP between the groups at M20. However, this difference is within the limits for this canine species (TEBALDI et al., 2012). Though propofol and isoflurane are known to cause hypotension and respiratory depression (BARBOSA, 2007; BORGES et al., 2008), no such effects were observed in this study. The effect of these drugs is dose-dependent and their side effects can be reduced by a combination of drugs or anesthetic techniques, as employed in this study (TONNER, 2005; BORGES et al., 2008). We used the recommended dose of propofol with premedication and the concentration of isoflurane was below its minimum alveolar concentration, which is 1.4 v% (MASTROCINQUE et al., 2012). The anesthetic concentration varies with the methodology and drugs used. Bosmans et al. (2011) maintained dogs under anesthesia using 1.8 v% isoflurane during orthopedic surgery along with epidural methadone and ropivacaine or a combination of methadone-ropivacaine. While Mastrocinque et al. (2012) used 1.4 v% isoflurane in bitches undergoing OSH along with ED tramadol combined with lidocaine. According to Valadão et al. (2002) and Natalini et al. (2011), general anesthesia combined with locoregional epidurally administered prophylactics with opioids and local anesthetics decreases inhalational anesthetic concentration required to maintain adequate anesthesia during the surgical procedure. This hypothesis is verified by the results from the GTR group, where a significant reduction in FEISO at time points related to surgical stimuli (M25 to M45) is observed compared to other groups.

Table 1. Mean and standard deviation values of body temperature (T, °C), heart rate (HR), systolic blood pressure (SBP), respiratory rate (F), carbon dioxide at the end of exhalation ($ETCO_2$), and oxyhemoglobin saturation (SpO_2) in bitches undergoing ovariohysterectomy under isoflurane anesthesia combined with epidural lumbosacral block using tramadol (GT group), ropivacaine (GR group) or a combination of GT-GR (GTR group) - Cuiabá / MT – 2014.

Variáble	Group	MB	MMPA	M0	M20	M25	M30	M45	M60	M120	M180	M240	M300	M360	M420
T°C (ºC)	GT	38,5±0,5	38,4±0,4	38,0±0,4	37,6±0,4	37,5±0,6	37,65±0,7	37,5±0,6	37,5±0,5	37,6±0,5	38±0,2	38±0,1	38,1±0,1	38,2±0,2	38,1±0
	GR	38,7±0,4	38,5±0,4	37,8±0,5	37,8±0,5	37,9±0,5	37,95±0,5	37,9±0,6	37,9±0,6	38,0±0,4	38,5±0,3	38,4±0,4	NA	NA	NA
	GTR	39,1±0,2	38,7±0,4	38,1±0,6	37,7±0,8	37,7±0,7	37,75±0,7	37,7±0,6	37,7±0,6	37,9±0,5	38,1±0,4	38,1±0,4	38,3±0,3	38,5±0,2	38,5±0,2
HR (bpm)	GT	120±15	107±15	110±10	109±12	108±8	109±11	108±6	112±14	114±8^{A}	132±29	127±20^{A}	129±34	132±40	132±0
	GR	126±15^{a}	110±16^{a}	108±11^{a}	111±13^{a}	112±13^{a}	110±16^{a}	109±13^{a}	107±19^{a}	129±18^{aB}	145±21^{b}	170±14^{bB}	NA	NA	NA
	GTR	126±9	111±10	107±12	111±16	110±18	102±18	104±10	107±13	109±10^{A}	121±15	118±13^{A}	123±15	132±21	130±21
SBP (mmHg)	GT	175±20	150±17	135±24	148±23^{A}	136±25	134±20	130±14	154±15	171±27	183±20	168±19	192±28	199±42	200±0
	GR	162±20^{a}	142±21^{a}	138±20^{a}	144±28^{aA}	139±29^{a}	131±23^{a}	127±24^{a}	149±13^{a}	180±35^{b}	184±39^{b}	197±3^{b}	NA	NA	NA
	GTR	181±31^{a}	164±16^{a}	140±38^{b}	121±13^{bB}	126±19^{b}	118±17^{b}	121±17^{b}	151±23^{a}	166±38^{a}	166±38^{a}	182±31^{a}	181±23^{a}	186±20^{a}	195±25^{a}
f (mpm)	GT	35±7^{a}	21±3^{a}	14±4^{b}	13±4^{b}	12±5^{b}	12±3^{b}	12±4^{b}	23±5^{a}	25±7^{a}	31±15^{aA}	20±0^{aA}	25±5^{a}	34±9^{a}	33±0^{a}
	GR	37±7^{a}	23±5^{b}	11±4^{c}	14±5^{c}	12±3^{c}	12±3^{c}	12±3^{c}	22±8^{b}	32±9^{a}	62±58^{dB}	60±28^{dB}	NA	NA	NA
	GTR	33±9^{a}	21±5^{b}	12±6^{b}	14±5^{b}	16±9^{b}	14±7^{b}	13±6^{b}	18±5^{b}	21±3^{b}	28±8^{aA}	30±10^{aA}	30±10^{a}	32±10^{a}	33±10^{a}
$ETCO_2$ (mmHg)	GT	NA	NA	41±4	39,87±3	39,75±4	41,12±5	40,5±4	NA	NA	NA	NA	NA	NA	NA
	GR	NA	NA	38,5±3	40,62±4	40,62±4	40,62±4	39,62±4	NA	NA	NA	NA	NA	NA	NA
	GTR	NA	NA	40,75±4	39,62±4	41,37±3	41,5±4	40,87±4	NA	NA	NA	NA	NA	NA	NA
SpO_2 (mmHg)	GT	NA	NA	98,87±1	99,5±0,7	99,37±0,5	99,87±0,3	99,5±0,7	NA	NA	NA	NA	NA	NA	NA
	GR	NA	NA	99,25±1	99±0,7	99,25±1	99,12±1	99,5±0,5	NA	NA	NA	NA	NA	NA	NA
	GTR	NA	NA	98,5±1	99,62±0,5	99,62±0,5	99,5±0,7	99,12±1	NA	NA	NA	NA	NA	NA	NA

Means followed by the same lowercase letters in the lines do not differ significantly from each other (Scott-Knot test, $p < 0.05$). Means followed by the same capital letters in columns do not differ significantly from each other (Scott-Knot test, $p < 0.05$).

NA = Not Rated; MB = Basal moment; MMPA = 15 minutes after premedication; M0 = the time of application of epidural anesthesia; M20 - M45 = time in minutes after application of epidural anesthesia and surgery related stimuli; M60 - M420 = time in minutes after application of epidural anesthesia.

Table 2. Mean values and standard deviations of the partial pressure of oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), oxyhemoglobin saturation in arterial blood (SaO_2), hydrogen potential (pH), and end-tidal isoflurane (FEISO) in bitches submitted to ovariohysterectomy under isoflurane anesthesia associated with epidural lumbosacral block with tramadol (GT), ropivacaine (GR), or their association (GTR) - Cuiabá / MT - 2014

Variáble	Group	MB	MMPA	M0	M20	M25	M30	M45	M60	M120	M180	M240	M300	M360	M420
PaO_2 (mmHg)	GT	NA	NA	497±102^{a}	NA	436±91^{a}	NA	467±131^{a}	NA	97±20^{b}	NA	NA	NA	NA	NA
	GR	NA	NA	522±52^{a}	NA	490±68^{a}	NA	511±53^{a}	NA	106±5^{b}	NA	NA	NA	NA	NA
	GTR	NA	NA	521±37^{a}	NA	510±74^{a}	NA	506±77^{a}	NA	105±9^{b}	NA	NA	NA	NA	NA
$PaCO_2$ (mmHg)	GT	NA	NA	43±4^{a}	NA	41±4^{a}	NA	43±4^{a}	NA	36±2^{b}	NA	NA	NA	NA	NA
	GR	NA	NA	41±6^{a}	NA	42±3^{a}	NA	41±4^{a}	NA	32±3^{b}	NA	NA	NA	NA	NA
	GTR	NA	NA	43±7^{a}	NA	43±3^{a}	NA	43±3^{a}	NA	35±2^{b}	NA	NA	NA	NA	NA
$SatO_2$ (%)	GT	NA	NA	98±0,4^{a}	NA	99±0,4^{a}	NA	98±0,3^{a}	NA	94±3^{bA}	NA	NA	NA	NA	NA
	GR	NA	NA	99±0,3^{a}	NA	99±0,3^{a}	NA	99±0,5^{a}	NA	96±1^{bB}	NA	NA	NA	NA	NA
	GTR	NA	NA	99±0,5^{a}	NA	99±0,4^{a}	NA	99±0,5^{a}	NA	96±1^{bB}	NA	NA	NA	NA	NA
pH (unid.)	GT	NA	NA	7,35±0,05	NA	7,39±0,05	NA	7,39±0,04	NA	7,41±0,06	NA	NA	NA	NA	NA
	GR	NA	NA	7,39±0,04	NA	7,41±0,04	NA	7,39±0,03	NA	7,41±0,11	NA	NA	NA	NA	NA
	GTR	NA	NA	7,37±0,05	NA	7,38±0,05	NA	7,39±0,04	NA	7,39±0,03	NA	NA	NA	NA	NA
$_{FE}ISO$ (V%)	GT	NA	NA	1,34±0,1^{a}	1,10±0,23^{b}	1,14±0,15^{bB}	1,13±0,14^{bB}	1,13±0,1^{bB}	NA	NA	NA	NA	NA	NA	NA
	GR	NA	NA	1,27±0,08	1,22±0,16	1,20±0,18^{B}	1,17±0,22^{B}	1,17±0,2^{B}	NA	NA	NA	NA	NA	NA	NA
	GTR	NA	NA	1,24±0,13^{a}	1,09±0,26^{a}	0,87±0,1^{bA}	0,97±0,15^{bA}	0,99±0,1^{bA}	NA	NA	NA	NA	NA	NA	NA

Means followed by the same lowercase letters in the lines do not differ significantly from each other (Scott-Knot test, $p < 0.05$). Means followed by the same capital letters in columns do not differ significantly from each other (Scott-Knot test, $p < 0.05$).

NA = Not Rated; MB = Basal moment; MMPA = 15 minutes after premedication; M0 = the time of application of epidural anesthesia; M20-M45 = time in minutes after application of epidural anesthesia and surgery related to stimuli; M60-M420 = time in minutes after application of epidural anesthesia.

The absence of cardiopulmonary changes between M20 and M45 reflects the elimination of nociceptive stimuli via the blockade of sympathetic fibers in the ED space by the local anesthetic. Tramadol, which is an atypical opioid, can also block sodium channels in sympathetic fibers (JONES, 2001; KARGI et al., 2008; VALVERDE, 2008; SMITH; LAUFER, 2014; SOUZA et al., 2013). The doses and drugs used in the three groups were equally effective in controlling transoperative pain following OSH, as inferred from the observed tachycardia, tachypnea, or hypertension. According to Adami et al. (2012), a similar dose of ropivacaine (1.0 mg kg^{-1}, ED) combined with isoflurane did not produce sufficient analgesia during invasive orthopedic surgery. On the other hand, in an experimental cranial cruciate ligament replacement surgery, isolated ED tramadol at a dosage of 1.0 mg kg-1 was efficient (GUEDES et al., 2002). Other authors reporting on studies using ropivacaine and tramadol alone or in combination did not consider the analgesic effect during the transoperative period, and evaluated only the postoperative period (PAOLOZZI et al., 2011; MASTROCINQUE et al., 2012; MORGAZ et al., 2013; SOUZA et al., 2013).

Hypothermia may occur during anesthesia due to the action of drugs on the thermoregulatory center (CASSU et al., 2008; SILVA et al., 2008), reduction of body metabolism (EGER, 1984), and sympathetic blockade caused by ED anesthesia (COUSINS; MATHER, 1984; CASSU et al., 2008; SILVA et al., 2008). It can also occur due to exposure of the abdominal cavity (ISHIY et al., 2002; CASSU et al., 2008). Hypothermia can reduce the cellular and humoral immunity and oxygen supply to peripheral tissues, thereby increasing the incidence of infection. It is, therefore, recommended that the body temperature should be maintained within the proper range using suitable alternatives (CORTOPASSI; FANTONI, 2010). In this study, the body temperatures were maintained between 37.5 and 39.5 °C for anesthetized animals using a thermal mattress during the transoperative period. The short duration of the surgical procedure is also an important factor in maintaining the temperature. This method of maintaining body temperature was also used by Mastrocinque et al. (2012) to maintain the body temperature above 37.5 °C in animals subjected to inhalation anesthesia combined with ED anesthesia during OSH. The elevation of temperature, the use of thermal blankets or mattresses in contact with the patient, as well as the infusion of heated solutions can also be used (CORTOPASSI; FANTONI, 2010). Failure to maintain the body temperature can cause hypothermia even when thermal mattresses are used in an operating room maintained at low temperatures (SILVA et al., 2008; NATALINI et al., 2011; CASSU et al., 2008). In this study, in addition to the use of a thermal mattress, the temperature was increased by interrupting the cooling when the body temperature of the animal reduced.

During the postoperative period, a subjective method known as EVA was used for the assessment of pain. Other researchers (CARREGARO et al., 2010, POHL et al., 2011; ADAMI et al., 2012; MORGAZ et al., 2013) have used the EVA scale in similar studies. The EVA scale is related to the physiological parameters FC and PAS in order to minimize the errors during interpretation (LANDA, 2012). The pain is assessed before and after the administration of the drug by the same observer who was blinded to the treatments (CARREGARO et al., 2010; POHL et al., 2011, 2012; PAOLOZZI et al., 2011; SOUZA et al., 2013).

Table 1 shows that the HR values at M120 and M240 and the F values at M180 and M240 are higher for the GR group. Similarly, the EVA values are also high at these time points for the GR group (Table 3). The lower analgesic efficiency is further verified by the largest rescue analgesia percentage at the M60 time point (Table 4). No further evaluations were performed from the M300 time point, because 100% of the animals had already received rescue analgesic. The combination of tramadol with ropivacaine (GTR group) provided longer analgesia time since at the end of the evaluation, only 37.5%

of the animals had received analgesia rescue, while in the tramadol group (GT) this percentage was 87.5%. There was a statistically significant difference between the postoperative analgesia time in the three groups (105, 217, and 382 min for the GR, GTR and GTR groups, respectively) (Table 5). These results confirm the findings obtained by Valadão et al. (2002), who reported that the combination of opioids with local anesthetics acts on receivers at different locations, and prolongs the analgesic period. The values for rescue analgesia were based on an increase of at least 20% in HR and SBP from baseline values and an EVA degree equal to five (BRONDANI et al., 2004; CASSU et al., 2008; CARREGARO et al., 2010; NATALINI et al., 2011; POHL et al., 2012). The animals in the GT group showed a duration of analgesia similar to that reported by Guedes et al. (2002), who used ED tramadol (1 mg·kg^{-1}) in dogs undergoing cranial cruciate ligament replacement and observed an analgesic effect for four hours. However, the method used by the authors to evaluate analgesia during the postoperative period is not known. Paolozzi et al. (2011) used tramadol at three different doses (1, 2, and 4 mg·kg^{-1}, IR) and observed analgesia for 12 h (evaluated using a composite scale) in dogs that underwent OSH. Vettorato et al. (2010) used tramadol at a dose of 2 mg·kg^{-1}, administered IV, and achieved satisfactory analgesia for 8 h in dogs undergoing orthopedic surgery (evaluated by the Glasgow scale). The differences in the duration of analgesia observed by different researchers can be attributed to the use of different scales for evaluation and surgical stimulus rather than the doses and routes (POHL et al., 2011; TEIXEIRA et al., 2013; REGALIN et al., 2014).

Table 3. Mean values of pain intensity in bitches, measured using the visual analogue scale (VAS) following ovariohysterectomy under isoflurane anesthesia combined with epidural lumbosacral block using tramadol (GT group), ropivacaine (GR group), or a combination of GT-GR (GTR group) - Cuiaba / MT – 2014.

	M60	M120	M180	M240	M300	M360	M420
GT	1	2	2.85	1.25	2.5	3.66	3.71
GR	1.62	2.85	3.5	5	NA	NA	NA
GTR	0.5	0.62	0.5	1	1.12	2.12	2.16

In the GR group, the mean duration of analgesia is identical to that observed by Feldman et al. (1996) cited in Albuquerque et al. (2010). However, the duration is shorter than that reported by Adami et al. (2012), which was 150 min in dogs undergoing orthopedic procedures (evaluated using the EVA and Glasgow scales). Nevertheless, the observed duration is similar to the mean duration of analgesia provided by ropivacaine (VALVERDE, 2008; MARUCIO; COTES, 2012). In case of the combination of ropivacaine with opioids, the mean duration of analgesia observed in this study is about 6 h. This is longer than that reported by Silva et al. (2008), who used a combination with tramadol (2 mg·kg^{-1}, DI) and observed a 4-h duration of analgesia in animals (evaluated through the Foley catheter 24 introduced via the rectum to the descending colon). Ropivacaine (0.3 ml·kg^{-1}, DI) combined with butorphanol (0.1 mg·kg^{-1}, DI) produced analgesia for an intermediate duration (308 min) in dogs subjected to OSH (ALBUQUERQUE et al., 2010). Analgesia was maintained for longer durations when combined at a higher dose (0.26 mL·kg^{-1}, ED) with morphine (0.1 mg·kg^{-1}, ED) in cats subjected to the same surgical procedure (evaluated using multidimensional scaling) (REGALIN et al., 2014).

Table 4. Descriptive analysis of the number of animals requiring postoperative analgesic rescue, during the experimental period (M60 to M420), using morphine and meloxicam, based on an evaluation using the visual analog scale (VAS). Bitches were subjected to ovariohysterectomy under isoflurane anesthesia combined with epidural lumbosacral block using tramadol (GT group), ropivacaine (GR group) or a combination of GT-GR (GTR group) - Cuiabá / MT – 2014.

	M60	M120	M180	M240	M300	M360	M420	Total
	---------- Animals that received rescue analgesia (%) ----------							
GT	0	12.5	37.5	0	12.5	25	0	87.5
GR	12.5	37.5	25	25	0	0	0	100
GTR	0	0	0	0	0	25	12.5	37.5

Table 5. Mean and standard deviation of analgesia duration during the postoperative period (M60 to M420), evaluated using the visual analog scale (VAS), in bitches subjected to ovariohysterectomy under isoflurane anesthesia combined with epidural lumbosacral block using tramadol (GT group), ropivacaine (GR group) or a combination of GT-GR (GTR group) - Cuiabá / MT – 2014.

Animal	Adequate analgesia time (min)
GT	217.5 ± 119^{A}
GR	105 ± 53^{B}
GTR	382.5 ± 54^{C}

Means followed by the same capital letters do not differ significantly from each other (Scott-Knot test, $p < 0.05$).

ED anesthesia is a safe and easy technique that provides adequate analgesia for retroumbilical surgical procedures. The duration of analgesia varies depending on the drug and the volume used (TONNER, 2005; REGALIN et al., 2014). This technique should be employed more frequently in veterinary medicine, particularly in patients with a higher risk under general anesthesia, since it reduces the doses of such drugs.

Conclusions

The drugs used in this study can be considered safe and effective for the surgical technique in question due to cardiorespiratory stability and transoperative analgesia. In addition, the combination of ropivacaine and tramadol provided a greater reduction in inhaled anesthetic doses and better analgesia during the postoperative period.

References

ADAMI, C.; VERES-NYEKI, K.; SPADAVECCHIA, C.; RYTZ, U.; BERGADANO, A. Evaluation of peri-operative epidural analgesia with ropivacaine, ropivacaine and sufentanil, and ropivacaine, sufentanil and epinephrine in isoflurane anesthetized dogs undergoing tibial plateau levelling osteotomy. *The Veterinary Journal*, London, v. 194, n. 2, p. 229-234, 2012.

ALBUQUERQUE, V. B.; SOUZA, T. F. B.; VIVAN, M. C. R.; FERREIRA, J. Z.; FRADE, M. C.; PERRI, S. H. V.; OLIVA, V. N. L. S. Influência do butorfanol sobre os períodos de latência e de ação da ropivacaína pela via peridural na ovariossalpingohisterectomia em cadelas. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, Belo Horizonte, v. 62, n. 4, p. 806-811, 2010.

ANDRADE, A. Fatores que influenciam no resultado do experimento animal. In: ANDRADE, A.; PINTO, S. C.; OLIVEIRA, R. S. *Animais de laboratório*: criação e experimentação. Rio de Janeiro: Editora Fiocruz, 2002. p. 289-294.

ARENA, G.; BOTELHO, A.; EVARISTO, B.; MORAIS, P. V.; NEGRI, D. D. Fenotiazínicos: usos, efeitos e toxicidade em animais de grande e pequeno porte. *Revista Científica Eletronica de Medicina Veterinária*, Garça, Ano 7, n. 12, p. 00-00, 2009.

BARBOSA, F. T. Síndrome da infusão do propofol. *Revista Brasileira de Anestesiologia*, Rio de Janeiro, v. 57, n. 5, p. 539-542, 2007.

BASSO, P. C.; RAISER, A. G.; CARREGARO, A. B.; MULLER, D. C. M. Analgesia transoperatória em cães e gatos. *Clínica Veterinária*, São Paulo, Ano 13, n. 77, p. 62-68, 2008.

BORGES, P. A.; NUNES, N.; BARBOSA, V. F.; CONCEIÇÃO, E. D. V.; NISHIMORI, C. T. D.; PAULA, D. P.; CARARETO, R.; THIESEN, R.; SANTOS, P. A. C. Variáveis cardiorrespiratórias, índice biespectral e recuperação anestésica em cães anestesiados pelo isofluorano, tratados ou não com tramadol. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, Belo Horizonte, v. 60, n. 3, p. 623-619, 2008.

BOSMANS, T.; SCHAUVLIEGE, S.; GASTHUYS, F.; DUCHATEAU, L.; MARCILLA, M. G.; GADEYNE, C.; POLIS, I. Cardiovascular effects of epidural administration of methadone, ropivacaine 0,75% and their combination in isofluorane anaesthetized dogs. *Veterinary Anaesthesia and Analgesia*, Oxford, v. 38, n. 2, p. 146-157, 2011.

BRONDANI, J. T.; NATALINI, C. C.; RAISER, A. G.; MAZZANTI, A.; PRATI, L. Analgesia epidural com clonidina ou romifidina em cães submetidos à cirurgia coxofemoral. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, Belo Horizonte, v. 56, n. 2, p. 175-182, 2004.

CARREGARO, A. B.; FREITAS, G. C.; MARQUES, J. S.; TREIN, T. A.; POHL, V. H.; SALBEGO, F. Z.; RAISER, A. G. Efeitos cardiorrespiratórios e analgésicos da cetamina por via epidural, por infusão intravenosa contínua ou pela associação de ambas, em cães submetidos à osteossíntese de fêmur. *Ciência Rural*, Santa Maria, v. 40, n. 7, p. 1583-1589, 2010.

CASSU, R. N.; STEVANIN, H.; KANASHIRO, C.; MENEZES, L. M. B.; LAPOSY, C. B. Anestesia epidural com lidocaína isolada e associada ao fentanil para realização de ovariosalpingo-histerectomia em cadelas. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, Belo Horizonte, v. 60, n. 4, p. 825-831, 2008.

CORTOPASSI, S. R. G.; FANTONI, D. T. Medicação pré-anestésica. In: FANTONI, D. T.; CORTOPASSI, S. R. G. *Anestesia em cães e gatos.* 2. ed. São Paulo: Roca, 2010. p. 217-227.

COUSINS, M. J.; MATHER, L. E. Intrathecal and epidural administration of opioids. *Anesthesioly*, Philadelphia, v. 61, n. 3, p. 276-310, 1984.

EGER, E. T. The pharmacology of isoflurane. *British Journal of Anaesthesia*, Oxford, v. 56, n. 1, p. 71-99, 1984.

FELDMAN, H. S.; DVOSKIN, S.; ARTHUR, G. R.; DOUCETTE, A. M. Antinociceptive and motor-blocking efficacy of ropivacaína and bupivacaine after epidural administration in the dog. *Regional Anesthesia and Pain Medicine*, Philadelphia, v. 21, n. 4, p. 318-325, 1996.

GUEDES, A. G. P.; NATALINI, C. C.; ALVES, S. D. L.; OLIVEIRA, S. T. Tramadol via epidural em cães submetidos à substituição do ligamento cruzado cranial. *Ciência Rural*, Santa Maria, v. 32, n. 2, p. 345-346, 2002.

ISHIY, H. M.; LUNA, S. P. L.; GONÇALVES, R. C.; CRUZ, M. L. Uso da lidocaína isolada ou associada à quetamina ou ao butorfanol, em anestesia epidural em cadelas submetidas à ovariosalpingohisterectomia. *Revista Brasileira de Ciência Veterinária*, Niterói, v. 9, n. 1, p. 125-127, 2002.

ITAMI, T.; TAMARU, N.; KAWASE, K.; ISHIZUKA, T.; TAMURA, J.; IYOSHI, K.; UMAR, M. A.; INOUE, H.; YAMASHTA, K. Cardiovascular effects of tramadol in dogs anesthetized with sevoflurane. *Journal of Veterinary Medical Science*, Tokyo, v. 73, n. 12, p. 1603-1609, 2011.

JONES, R. S. Epidural analgesia in the dog and cat. *The Veterinary Journal*, London, v. 161, n. 2, p. 123-131, 2001.

KARGI, E.; BABUCCU, O.; ALTUNKAYA, H.; HOSNUTER, N.; OZER, Y.; BABUCCU, B.; PAYASLI, C. Tramadol as a local anaesthetic in tendon repair surgery of the hand. *Journal of International Medical Research*, London, v. 36, n. 5, p. 971-978, 2008.

LANDA, L. Pain in domestic animals and how to assess it: a review. *Veterinarni Medicina,* Praga, v. 57, n. 4, p. 185-192, 2012.

MARUCIO, R.; COTES, L. Fármacos de uso espinhal. In: FANTONI, D. *Tratamento da dor na clínica de pequenos animais.* Rio Janeiro: Elsevier, 2012. p. 181-194.

MASTROCINQUE, S.; ALMEIDA, T. F.; TATARUNAS, A. C.; IMAGAWA, V. H.; OTSUKI, D.; MATERA, J. M.; FANTONI, D. T. Comparison of epidural and systemic tramadol for analgesia following ovariohysterectomy. *American Animal Hospital Association*, Lakewood, v. 48, n. 5, p. 311-319, 2012.

MCMILLAN, C. J.; LIVINGSTON, A.; CLARK, C. R.; DOWLING, P. M.; TAYLOR, S. M.; DUKE, T.; TERLINDEN, R. Pharmacokinetics of intravenous tramadol in dogs. *Canadian Journal of Veterinary Research*, Ottawa, v. 72, n. 4, p. 325-331, 2008.

MORGAZ, J.; NAVARRETE, R.; MUÑOZ-RASCÓN, P.; DOMÍNGUEZ, J. M.; FERNÁNDEZ-SAMIENTO, J. A.; GÓMEZ-VILLAMANDOS, R. J.; GRANADOS, M. M. Postoperative analgesic effects of dexketoprofen, buprenorphine and tramadol in dogs undergoing ovariohysterectomy. *Research in Veterinary Science*, Oxford, v. 95, n. 1, p. 278-282, 2013.

NATALINI, C. C.; CRUZ, F. S. F.; BOPP, S. Analgesia epidural com clonidina ou sufentanil epidural em cadelas submetidas à ovariosalpingohisterectomia sob anestesia geral inalatória. *Acta Scientiae Veterinariae*, Porto Alegre, v. 39, n. 4, p. 992-1001, 2011.

PAOLOZZI, R. J.; CASSU, R. N.; CRUZ, F. S. F.; PARRILHA, L. R. Diferentes doses de tramadol em cães: ações analgésicas, sedativas e sobre o sistema cardiorrespiratório. *Ciência Rural*, Santa Maria, v. 41, n. 8, p. 1417-1423, 2011.

PEREZ, T. E.; GRUBB, T. L.; GREENE, S. A.; MEYER, S.; VALDEZ, N.; BINGMAN, J.; FARNSWORTH, R. Effects of intratesticular injection of bupivacaine and epidural administration of morphine in dogs undergoing castration. *Journal of the American Veterinary Medical Association*, Schauburg, v. 242, n. 5, p. 631-642, 2013.

POHL, V. H.; CARREGARO, A. B.; LOPES, C.; GARLET, C.; MARQUES, J. S. Correlação entre as escalas visual analógica, de Melbourne e filamentos de Von Frey na avaliação da dor pós-operatória em cadelas submetidas à ovariosalpingohisterectomia. *Ciência Rural*, Santa Maria, v. 41, n. 1, p. 154-159, 2011.

POHL, V. H.; CARREGARO, A. B.; LOPES, C.; GEHRCKE, M. I.; MULLHER, D. C. M.; GARLET, C. D. Epidural anesthesia and postoperatory analgesia with alpha-2 adrenergic agonists and lidocaine for ovariohysterectomy in bitches. *Canadian Journal of Veterinary Research,* Ottawa, v. 76, n. 3, p. 215-220, 2012.

REGALIN, D.; MORESCO, M.; PADILHA, V. S.; TOCHETO, R.; OLESKOVICZ, N. Efeitos cardiovasculares e analgésicos da administração epidural de ropivacaína isolada ou associada à morfina, em felinos. *Ciência Rural*, Santa Maria, v. 44, n. 12, p. 2228-2235, 2014.

SILVA, B. M.; MATSUBARA, L. M.; ALBUQUERQUE, V. B.; MAIA, C. A. A.; OLIVA, V. N. L. S. Ropivacaína isolada e associada ao fentanil ou ao tramadol administrados ela via epidural em cães. *Ciência Rural*, Santa Maria, v. 38, n. 8, p. 2197-2202, 2008.

SMITH, H. S.; LAUFER, A. Opioid induced nausea and vomiting. *European Journal of Pharmacology*, Amsterdam, v. 722, n. 5, p. 67-78, 2014.

SOUZA, M. D. I.; MENCALHA, R.; WAKOFF, T. I.; SOUSA, C. A. S.; SCHERER, P. O. Estudo comparativo entre a utilização de Levobupivacaína 0,5% e Ropivacaína 1% na anestesia epidural lombossacra em gatos. *Semina: Ciências Agrárias*, Londrina, v. 34, n. 6, p. 2925-2936, 2013.

TEBALDI, M.; LOURENÇO, M. L. G.; MACHADO, L. H. A.; SUDANO, M. J.; CARVALHO, L. R. Estudo da pressão arterial pelo método indireto oscilométrico (petmap®) em cães domésticos não anestesiados. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, Belo Horizonte, v. 64, n. 6, p. 1456-1464, 2012.

TEIXEIRA, R. C. R.; MONTEIRO, E. R.; CAMPAGNOL, D.; COELHO, K.; BRESSAN, T. F.; MONTEIRO, B. S. Effects of tramadol alone, in combination with meloxicam or dipyrone, on postoperative pain and the analgesic requirement in dogs undergoing unilateral mastectomy with or without ovariohysterectomy. *Veterinary Anaesthesia and Analgesia*, Oxford, v. 40, n. 6, p. 1-8, 2013.

TONNER, P. H. Balanced anaesthesia today. *Best Practice e Research Clinical Anaesthesiology*, Amsterdam, v. 19, n. 3, p. 475-484, 2005.

VALADÃO, C. A. A.; DUQUE, J. C.; FARIAS, A. Administração epidural de opióides em cães. *Ciência Rural*, Santa Maria, v. 32, n. 2, p. 347-355, 2002.

VALVERDE, A. Epidural analgesia and anesthesia in dogs and cats. *Veterinary Clinic of North America Small Animal Practice*, Philadelphia, v. 38, n. 6, p. 1205-1230, 2008.

VAN DE VELDE, M.; DREELINCK, R.; DUBOIS, J.; KUMAR, A.; DEPREST, J.; LEWI, L.; VANDERMEERSCH, E. Determination of the full dose-response relation of intrathecal bupivacaine, levobupivacaine, and ropivacaine, combined with sufentanil, for labor analgesia. *Anesthesiology*, Filadélfia, v. 106, n. 1, p. 149-156, 2007.

VETTORATO, E.; ZONCA, A.; ISOLA, M.; VILLA, R.; GALLO, M.; RAVASIO, G.; BECCAGLIA, M.; MONTESISSA, C.; CAGNARDI, P. Pharmacokinetics and efficacy of intravenous and extradural tramadol in dogs. *Veterinary Journal*, Londres, v. 183, n. 3, p. 310-315, 2010.