Extradural anesthesia with lidocaine combined with fentanyl or methadone to ovariohisterectomy in dogs[1]

Miriely Steim Diniz[I], Gláucia Prada Kanashiro[II], Camila Angela Bernardi[II], Gabriel Montoro Nicácio[III], Renata Navarro Cassu[IV]

[I]VMD, Resident, Department of Veterinary Surgery and Anestesiology, Scholl of Veterinary Medicine, Oeste Paulista University (UNOESTE), Presidente Prudente-SP, Brazil. Acquisition of data, helped with technical procedures, collection and processing of study informations, manuscript writing.

[II]Master, Full Professor, Department of Veterinary Surgery and Anestesiology, Scholl of Veterinary Medicine, UNOESTE, Presidente Prudente-SP, Brazil. Helped with technical procedures, collection and processing of study informations.

[III]Full Professor, Department of Veterinary Surgery and Anestesiology, Scholl of Veterinary Medicine, UNOESTE, Presidente Prudente-SP, Brazil. Helped with technical procedures.

[IV]PhD, Full Professor, Department of Veterinary Surgery and Anestesiology, Scholl of Veterinary Medicine, UNOESTE, Presidente Prudente-SP, Brazil. Mentor. Responsible for intellectual and scientific content of the study; statistical analysis; critical revision.

ABSTRACT

PURPOSE: To compare the cardiopulmonary effects and the quality of anesthesia of the extradural lidocaine in combination with fentanyl or morphine in bitches undergoing ovariohysterectomy.

METHODS: Sixteen female dogs, were sedated with intramuscular acepromazine (0.05mg kg^{-1}), followed by anesthetic induction with intravenous propofol (4mg kg^{-1}), to perform the lumbosacral puncture. The animals were randomly assigned to two treatments: T-F (n=8) extradural administration of fentanyl (5µg kg^{-1}), T-M (n=8) extradural administration of methadone (0.3mg kg^{-1}). In both treatment groups, opioids were combined with lidocaine, in order to make up a final volume of 0.4mL kg^{-1}. Heart rate (HR), respiratory rate (RR), systolic arterial blood pressure (SABP), intra-operative anesthetic supplementation, blood gases and adverse effects were investigated.

RESULTS: HR, arterial pH and blood gases did not differ between treatments at any time point. RR and SABP decreased after epidural anesthesia, but the values were in terms of the physiological range of dogs. Intra-operative anesthetic supplementation was required in 50% and 62.5% of the fentanyl and methadone treated dogs, respectively.

CONCLUSION: The extradural lidocaine in combination with fentanyl or morphine allowed cardiopulmonary stability, however sufficient sensitive blockade was not provided in 100% of the dogs.

Key words: Anesthesia, Epidural. Analgesics, Opioid. Lidocaine. Fentanyl. Methadone. Dogs.

Introduction

One of the most common elective surgical procedures performed in dogs is ovariohysterectomy (OHE). The procedure is normally carried under general anesthesia. Alternatively, extradural anesthesia is an attractive and inexpensive method for retro umbilical surgical procedures. Unlike other anesthetic techniques, extradural anesthesia produces minimal cardiovascular and respiratory depression[1].

In dogs have been reported maximal spread of anesthetic blockade until to fourth or sixth lumbar vertebra following lumbosacral extradural lidocaine[2-4] which is usually unsatisfactory to OHE, because the ovarian pedicle is innervated by third and fourth lumbar afferent nerves[5].

Thus, some studies have proposed the extradural administration of an opioide in combination with lidocaine in an attempt to spread the sensory blockade, optimizing the anesthesia to lower abdominal surgical procedures in dogs[6-9].

Morphine administered extradurally in combination with lidocaine provided safe and satisfactory anesthesia for performing OHE in 100% of the dogs, so that general supplemental anesthesia was not required[9]. Similar results were showed with extradural butorphanol plus lidocaine for dogs undergoing OHE[7]. In both studies, minimal adverse effects such as nausea, vomiting, and cardiopulmonary depression were reported.

However, despite these favorable results, there are relatively few studies about extradural anesthesia as a single technique for surgical procedures in dogs. The majority of the studies have focused on the effects of the extradural in combination with general anesthesia[10-14].

The objective of the present investigation was to compare the cardiopulmonary effects and the quality of extradural anesthesia with lidocaine in combination with fentanyl or methadone in bitches undergoing OHE.

Methods

This study was approved by the Institutional Animal Research Ethical Committee (protocol number 358), and permission for the participation of each dog was obtained from the owner. Sixteen healthy adult, crossbreed, female dogs, which weighed 4.5 to 15 kg were evaluated. Animals undergoing elective OHE were selected for this study using a physical examination and laboratory tests (complete blood cell count, urea, creatinine, alanine aminotransferase and aspartate aminotransferase).

After withdrawal of food and water for 12 and three hours, respectively, all dogs were sedated with 0.05mg kg^{-1} of acepromazine maleate (Acepran 0.2%, Univet, Sao Paulo, Brazil) administered intramuscular (IM). Twenty minutes after sedation, anesthesia was induced with 4 to 5mg kg^{-1} intravenously (IV) propofol (Propovan, Cristalia, Itapira, Brazil), to perform the lumbosacral puncture.

All dogs were prepared for extradural (ED) injection analgesia: hair in the lumbosacral area was clipped, and the dogs were placed in sternal recumbency. Each was randomly assigned to receive 5μg kg^{-1} of fentanyl (Fentanest, Cristalia, Itapira, Brazil) (T-F, n=8) or 0.3mg kg^{-1} of methadone (Metadon, Cristalia, Itapira, Brazil) (T-M, n=8) by the extradural route. In both treatments, the drugs were given in combination with lidocaine (Xilestesin 2% com vasoconstritor, Cristalia, Itapira, Brazil) to produce a total volume of 0.4mL kg^{-1}. ED injection was performed at the lumbosacral (L7-S1) space. Correct spinal needle placement was confirmed by a lack of resistance to injection[3]. The drugs were injected over a two minutes period.

Following the ED injection, the animals were maintained in sternal recumbency for 20 minutes, for the uniform distribution of the drugs in the epidural space and due to the latency period of the opioids and lidocaine. After this period, the anesthetic blockade was confirmed by absence of flexor-pinch reflex of pelvic limbs, once the dogs were already aware due to the short central depression induced by propofol. Thereafter, the animals were positioned in dorsal recumbency on a surgical bed for the OHE. All animals underwent routine OHE through a 2 -to 3- cm midline incision by the same experienced surgeon.

Ringer's lactate solution (10mL kg^{-1} h^{-1}) was infused IV using a peristaltic infusion pump (ST1000, Samtronic, Sao Paulo, Brazil) throughout the surgical procedure.

During the anesthetic procedure, oxygen saturation of hemoglobin (SpO$_2$%) and heart rate (HR) were continuously measured with pulse oximeter (VAMOS plus, Dräger, Sao Paulo, Brazil), with the sensor on the vulva. Systolic arterial blood pressure (SABP) was measured by noninvasive method using a Doppler ultrasonic (Doppler 841-A, Parks Medical Electronics, Las Vegas, EUA), with the width cuff about 40% of the circumference of the antebrachium. Respiratory rate (RR) was measured by observation of the thoracic movements for one minute. Measurements were made before premedication (Baseline), 15 minutes after premedication administration, five minutes and every ten minutes after the start of surgery.

Arterial blood samples were collected into heparinized syringes from the femoral artery, by puncture. All arterial blood gas samples were stored on ice and analyzed immediately on

as automated blood gas analyzer (Cobasp, modelo 121, Roche-Macromed, Sao Paulo, Brazil). Samples were corrected for body temperature. Arterial blood pH, carbon dioxide partial pressure ($PaCO_2$), oxygen partial pressure (PaO_2), arterial hemoglobin saturation (SaO_2), arterial bicarbonate concentration (HCO_3^{-1}) were determined before the pre-anesthetic medication was administered (Basaline), at the time of the ovarian pedicle clamping (IO), and at the end of the surgery (After OHE).

Supplemental anesthesia was provided with a propofol (5mg kg^{-1}) bolus if extradural anesthesia was unsatisfactory. Any dog showing signs of discomfort, based on an increase in heart rate and/or arterial blood pressure >20% of the baseline values[18], as well as sudden voluntary movements of the forelimbs or head. The total number of propofol doses and their intervals were recorded.

Duration of surgery and the post-anesthetic recovery were recorded as well as the occurrence of adverse effects such as nausea, vomiting and excitement.

Data were recorded as mean±SD. The data analyzed using an analysis of variance with the F test followed by Tukey's test using Graphpad software. Differences between treatments at each time point, differences in time for each treatment, and the interaction between treatment and time were investigated. A P-value less than 0.05 was considered significant.

Results

There were no differences (p>0.05) between the groups in terms of body weight (9±5 and 9.2±2.5 kg for the T-F and T-M groups, respectively) and surgical time (21±3 and 22±2 minutes for the T-F and T-M groups, respectively).

Heart rate, arterial pH, $PaCO_2$, PaO_2, SaO_2 and HCO_3^- did not differ between treatments at any time point (Tables 1 and 2).

Systolic arterial blood pressure did not change between treatment groups, except at five minutes after the start of the surgery, when this parameter was lower in T-F in comparison with T-M (Table 1).

Respiratory rate was not significantly different between treatment groups at any time after extradural administration. However, lower RR was observed at five, ten and 20 minutes after the start of OHE when compared with the baseline values in both groups (Table 1).

There was no significant difference in requirement for supplemental intra-operative anesthesia between treatment groups. Four of the eight dogs (50%) in the fentanyl group required propofol during the ovarian manipulation, compared with five (62.5%) in the methadone group.

Undesirable side effects were not observed in any of the dogs.

TABLE 1 - Heart rate (HR), respiratory rate (RR), systolic arterial blood pressure (SABP) in dogs treated with lidocaine in combination with fentanyl (T-F, n=8) or methadone (T-M).

Variable	Time (min)				
	Baseline	15	5^s	10^s	20^s
HR (beats min^{-1})					
T-F	115±30	104±15	119±25	92± 17	98±15
T-M	123±33	110±20	107±30	98±23	95±20
RR (breats min^{-1})					
T-F	40±24	28±10	19±6*	17±6*	16±5*
T-M	31±8	24±9	20±5*	18±3*	18±4*
SABP (mmHg)					
T-F	131±19	118±14	102±3*	113±19	110±16
T-M	141±18	120±12	114±5*#	114±12*	108±15*

Values are shown as mean±SD. *Significantly different from baseline values (p < 0.05). #Significantly different from T-F treatment (p < 0.05).
Times listed are baseline, 15 minutes following premedication (15), and 5, 10, 20 minutes following the start of surgery (5^s, 10^s, 20^s).

TABLE 2 - Arterial blood gases, pH and bicarbonate in dogs treated with lidocaine in combination with fentanyl (T-F, n=8) or methadone (T-M).

Variables	Baseline	IO	After OHE
pH			
T-F	7.38±0.03	7.38±0.03	7.36± 0.02
T-M	7.38±0.05	7.35±0.04	7.34±0.03
PaO_2 (mmHg)			
T-F	34±2	38±2	36±5
T-M	36±3	35±4	37±5
PaO_2 (mmHg)			
T-F	96±6	96±6	97±6
T-M	100±5	98±6	102±4
Sat_{O2} (%)			
T-F	98	96	97
T-M	97	96	97
HCO_3^- (mmol/L)			
T-F	18±2	21±3	21±3
T-M	19±3	20±3	22±2

Values are shown as mean±SD.
Times listed are baseline, IO: intra-operative period (at the time of the ovarian pedicle clamping) and after OHE: immediately after the end of the surgery.
$PaCO_2$: carbon dioxide partial pressure; PaO_2: oxygen partial pressure; HCO_3: bicarbonate

Discussion

The current study confirms previous reports in dogs, which have shown minimal cardiovascular changes after lidocaine in combination with different opioids administered by extradural route[4,7,8].

Opioid-induced cardiovascular depression is dose and administration route dependent[15]. The incidence of adverse effects is lower after extradural administration when compared with parenteral opioids[12,13]. In the current study, mild reduction was observed in systolic blood pressure after extradural injection in the both treatment groups, however hypotension (SABP<90mmHg) was not observed. This result supports the findings of Bosmans *et al.*[14] that reported reduction in blood pressure after ED methadone administration in dogs, however clinical values were maintained. Leibetseder *et al.*[13] showed moderate hypotension after ED methadone (0,3mg kg^{-1}) in combination with an isoflurane concentration of 1.0% in dogs, but median arterial blood pressure increased with surgical stimulation to values within the normal range. Similar results have been reported following ED fentanyl plus local anesthetic, with minimal cardiovascular changes in dogs undergoing elective OHE[6,16,17]. In addition, the premedication may have contributed to the reduction of blood pressure due to blockade of α_1- receptors by acepromazine maleate[18]. Moreover,

the cardiovascular effects of propofol are well documented. It transiently depresses arterial pressure and myocardial contractility similar to the thiobarbiturates[19]. Thus, both the administration of a bolus of propofol at the time of epidural needle placement and the additional doses required during the surgery may reduce the blood pressure.

In dogs, respiratory function is not impaired following extradural anesthesia, unless local anesthetic produce motor blockade of the phrenic nerve at cervical vertebra[1]. However, the use of epidural opioids, particularly morphine, has been associated with respiratory depression, mainly in people[15]. The mechanism of respiratory depression after epidural morphine seems to be related to morphine's low lipid solubility. In comparison with hydrophilic drugs, the rapid uptake of extradural lipophilic compounds reduces their capacity to cause late respiratory depression[20]. Leibetseder *et al.*[13] reported pronounced respiratory depression following methadone intravenous administration, while extradural methadone did not affect respiratory pattern in dogs. Similarly, previous publications have shown minimal changes in respiratory rate and blood gases following epidural fentanyl combined with lidocaine in dogs[6,8,16,17], which is in agreement with the results of the current study. All dogs had significantly lower respiratory rate following epidural injection, however, bradypnea was not observed. Additionally, arterial pH and blood gases remained

within the physiological range, suggesting that both treatments did not impair the ventilatory status.

Lidocaine has a rapid onset of action. Approximately 1mL of 2% lidocaine per 4.5kg of body weight will completely anesthetize the pelvic limbs and posterior abdomen within ten to 15 min after administration[1,2]. Similarly, the more lipophilic opioids such as methadone and fentanyl are able to cross the meninges quite rapidly, resulting in a short onset of action[15]. In human beings, the onset time of effect of ED methadone and fentanyl is about ten to 20 minutes[20]. Thus, in the current study, the surgery was started only 20 minutes after ED injection, when the anesthetic blockade was confirmed by absence of flexor-pinch reflex of pelvic limbs. However, despite the absence of the toe reflexes be associated with surgical anesthesia[1], supplemental propofol was required in 50% and 62.5% in fentanyl and methadone treated dogs, respectively. This result suggests that cranial dispersion of the drugs injected into epidural space was insufficient to reach the cranial lumbar dermatomes, impairing the ovarian manipulation. In dogs, the spread of sensitivity blockade to the upper third lumbar vertebra was showed just in 50% of the dogs following ED methadone plus lidocaine[4]. Similarly, in 40% of the dogs anesthetized with ED fentanyl in combination with lidocaine was necessary supplemental anesthesia during the ovarian clamping[8].

Both treatments provided satisfactory post-anesthetic recovery. No adverse effects were observed in the current study, which is in agreement with previous results reported in dogs following extradural opioids in combination with local anesthetics[4,6-8].

Conclusion

The extradural lidocaine in combination with fentanyl or morphine provides cardiopulmonary stability to dogs undergoing ovariohysterectomy. However, sensitivity blockade was not sufficient to ovarian manipulation in 100% of the dogs.

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Correspondence:
Renata Navarro Cassu
Faculdade de Medicina Veterinária-UNOESTE
Departamento de Cirurgia e Anestesiologia Veterinária
19067-175 Presidente Prudente – SP Brazil
Tel.: (55 18)3229-2077
navarro@unoeste.br
renavarro@uol.com.br

[1]Research performed at Veterinary Hospital, Department of Veterinary Surgery and Anestesiology, Faculty of Veterinary Medicine, Oeste Paulista University (UNOESTE), Presidente Prudente-SP, Brazil.