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Assessment of thermal response, cardiorespiratory parameters and post-operative analgesia in dogs undergoing ovariohysterectomy with different combinations of epidural analgesia and isoflurane

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Abstract This study aimed to evaluate the thermal response of the eyelids and lacrimal gland of the left eye (LETG) through infrared thermography (IRT), cardiorespiratory parameters, and their association with nociception and pain in bitches undergoing elective ovariohysterectomy (OVH) anesthetized with isoflurane and epidural analgesia. Twenty-one healthy bitches of different breeds were randomized into three groups receiving epidural blocks: GL (n=7), lidocaine (2 mg Kg^{-1}); GLF (n=7), lidocaine (2 mg Kg^{-1}) and fentanyl (3 µg Kg^{-1}); and GLM (n=7), lidocaine (2 mg Kg^{-1}) with morphine (0.1 mg Kg^{-1}). IRT and cardiorespiratory parameters were evaluated at baseline (E_{basal}), thirty minutes before anesthetic premedication, and at different surgical events: first incision (E_{Inc}), ligature and section of the left (E_{LoV}), and right (E_{RoV}) ovarian pedicle, ligature, and re-section of the cervix (E_{Ut}), and skin suture (E_{Sut}). The assessment of acute pain in the immediate post-operative period was registered at E_{1h}, E_{2h}, and E_{3h} using IRT, the Dynamic Interactive Visual Analogic Scale (DIVAS), and the University of Melbourne Pain Scale (UMPS) scales. The results showed a statistically significant decrease in the lower eyelid surface temperature (LELT) during E_{Inc} for GL (32.9°C ± 0.62), in comparison to GLF (34.2°C ± 0.62) and GLM (35.3°C ± 0.62) (P = 0.006). Regarding LETG, a significant increase (P = 0.03) in the IRT of E_{basal} (36.8°C ± 0.63) and E_{Inc} (36.1°C ± 0.63) for GLM was observed in comparison to the thermographic values for both perioperative events and groups. The GLM showed a significant decrease in IRT values of E_{RoV} at E3h in the upper and lower eyelids (P = 0.03 and P = 0.01, respectively). A progressive and significant reduction of the IRT values of LETG was also recorded in GLM, with differences in E_{RoV} (35.2 °C ± 0.63) (P = 0.02) and E_{3h} (35.3 °C ± 0.63) (P = 0.01). The cardiovascular parameters (SAP, DAP, and MAP) did not differ between treatments, but in GL, there was a significant difference (P = 0.01) during E_{Inc} and E_{Sut}, compared to E_{basal}. In the body temperature, E_{Inc} and E_{Sut} gradually decreased in all treatment groups (P = 0.01). In conclusion, hemodynamic and cardiorespiratory stability was associated with IRT readings and the absence of nociception. Changes in superficial temperature in the immediate post-operative period were lessened using isoflurane and epidural analgesia of lidocaine alone or in combination with pure opioids. These findings were clinically validated to the DIVAS and UMPS acute pain assessment scales.

Keywords: analgesia, dogs, epidural, lidocaine, opioids, thermography image

1. Introduction

For Nociception negatively impacts the recovery of animals subjected to anesthetic-surgical procedures. The perception of such harmful stimuli triggers a sympathetic physiological response by activating the hypothalamic-pituitary-adrenal axis (Finnerty et al 2013; Lai Carlo 2015). This condition has been described as surgical stress (Desborough 2000; Hernández-Avalos et al 2021a). This response is characterized, among other reactions, by autonomic hemodynamic reactivity, defined as increased heart rate and arterial blood pressure due to the neurosecretion of epinephrine, norepinephrine, cortisol, and other chemical mediators. In consequence, the stimulation of the Autonomic Nervous System (ANS) and its sympathetic nerve fibers causes a decrease in blood flow in non-essential organs and changes in respiratory patterns (Giannoudis et al

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2006; Stephenson 2014; Höglund et al 2016; Mansour et al 2017).

Therefore, pain recognition requires subjective criteria, such as behavior or body posture changes, and objective elements as physiological parameters or neuroendocrine responses (Matičić et al 2010; McMillan 2016). In animals, external factors such as fear or anxiety can cause changes in hemodynamic stability, and its differentiation from pain is challenging (Reid et al 2017).

Given that surgically-induced nociception causes hemodynamic instability (Mansour et al 2017), some studies have successfully used infrared images to detect and evaluate this phenomenon (Grossbard et al 2014). Research on humans has identified that facial expressions can reflect the degree of perceived pain (Prkachin and Solomon, 2008) and that a complementary technique, such as infrared thermography (IRT), helps in recognizing nociception and quantifying the autonomic response (Czaplik et al 2017).

Veterinary medicine is adopting IRT as a non-invasive tool for assessing animal autonomic activation following nociception and stress (Travain et al 2015; Mota-Rojas et al 2021a,b,c,d). This technique detects changes in surface circulation or dermal microcirculation (Childs, 2018) that reflect sympathetic activity and alterations in the surface temperature in individuals perceiving harmful stimuli (Stewart et al 2010; Zanghi 2016; Mota-Rojas et al 2021e,f,g; Mota-Rojas et al 2022a,b; Napolitano et al 2023). In essence, this tool assesses temperature changes (Küls et al 2017) and has been used to detect exercise-induced stress (Esteves Trindade et al 2019), transport-induced stress in sheep (Bartolomé et al 2019), to evaluate chronic pain (McQueen et al 2017), to predict infections in swine (Schaefer et al 2004), to assess neonatal thermostability (Villanueva-García et al 2021; Mota-Rojas et al 2022a; Gómez-Prado et al 2022; Lezama-García et al 2022; Napolitano et al 2023), to identify sick zoo animals (Mota-Rojas et al 2022b,c), and to discriminate anxiety from pain in dogs (Lush and Ijichi, 2018).

When used to study painful states, this technique has been associated with temperature decreases related to blood flow changes due to sympathetic vasoconstriction (Huggins and Rakobowchuk, 2019). However, some authors report increases in the surface temperature of specific regions due to an increase in cell metabolism triggered by inflammation (Grossbard et al 2014; Paranzini et al 2018; Repac et al 2020). In species such as cattle under painful procedures (e.g., orchiectomy), IRT was used in the lacrimal caruncle. In this specific anatomical region, the perception of pain and the stimulation of sympathetic fibers innervating the infraorbital blood vessels causes a significant decrease in its superficial temperature (Stewart et al 2008, 2009, 2010). This has also been reported in equines, validating this region for assessing the welfare of this species (Witkowska-Piłaszewicz et al 2021). In contrast, in humans, the lacrimal caruncle has not been associated with the activity of the ANS (Seixas and Ammer, 2019).

In dogs, it has been reported that the lacrimal caruncle has a moderate correlation with pain assessment scales after a surgical procedure such as an orchiectomy (Lush and Ijichi, 2018). The above suggests that the lacrimal caruncle is an accurate thermal window that can be evaluated through IRT, in which temperature fluctuations could be associated with stress and pain. This region already has a high density of blood capillaries and arteriovenous anastomoses that make it sensitive to thermal exchange with the environment, giving it the value of a thermal window (Mota-Rojas et al 2021). However, this particular window has some limitations that could affect its interpretation and results –e.g., the need to keep the eye open– (Zanghi, 2016). An alternative is to use the eyelid and tear gland (Czaplik et al 2017; Casas-Alvarado et al 2020). Current research aims to identify and validate diverse thermal windows (Loughin and Marino, 2007).

Implementing a suitable analgesic plan, particularly during a surgical procedure, is necessary to prevent the consequences of pain (Epstein et al 2015). Some articles suggest that the administration of pure opioids such as morphine and fentanyl provides superior analgesia compared to other analgesic drugs (Garcia-Pereira, 2018). However, respiratory depression and hypotension can be adverse effects of opioid administration (Mwangi et al 2018). To diminish the presentation of these outcomes, multimodal analgesia, known as the combination of different analgesic drugs to potentiate their effect, is suggested as an alternative to conventional pharmacological therapy. In this regard, the epidural administration of lidocaine in combination with pure opioids has been proposed to reduce perioperative pain in dogs (Steagall 2017).

This study hypothesized that combining lidocaine with pure opioids could mitigate the cardiovascular response associated with nociception and, consequently, the IRT readings in dogs undergoing elective ovariohysterectomy (OVH). This study evaluated the analgesic effect of epidural administration of lidocaine alone or combined with morphine or fentanyl in bitches subjected to elective OVH. For these, IRT from the eyelid and tear gland of the left eye was used, as well as cardiorespiratory parameters and two acute post-operative pain scales: Dynamic Interactive Visual Analogous Scale (DIVAS) and the University of Melbourne pain scale (UMPS).

2. Materials and Methods

2.1. Animals

Twenty-one healthy bitches of different breeds (17 mixed breeds, 1 Schnauzer, 1 Poodle, 1 Labrador, and 1 Basset hound) were admitted for elective OVH. Before admission, a complete pre-operative physical exam, blood cell counts, and biochemical serum and urine analyses were performed on every dog. The sample size estimation was carried out according to the procedure proposed by Charan and Biswan (2013) for clinical trials. The estimated sample size was 21.8 animals considering an alpha error of 0.05 and beta of 0.84, according to the following formula:

$$\text{Sample size} = \frac{2\text{SD}^2(Z_{\frac{\alpha}{2}} + Z_{\beta})2}{\text{d}^2}$$

According to their physical status, determined by the American Society of Anesthesiologists, only healthy animals or those classified with an anesthetic risk condition of ASA1 (Doyle et al 2020). We excluded brachiocephalic dogs (e.g., Boxer, Pug, Shih Tzu, Boston Terrier, and Bulldog) or with eyelid disorders. All surgeries were elective and approved under the informed consent of the owner. The average age of the bitches included in the study was 3 ± 1.5 years, with a mean body condition score of 3/5 ± 1.5 and a mean weight of 11.15 ± 2.5 kg.

2.2. Anesthetic-surgical procedure

All the animals were kept under fasting conditions without food or water for 6 hours before induction of general anesthesia. Aseptic catheter placement was performed in the cephalic vein to administer a Ringer lactate solution at an infusion velocity of 10 mL Kg^{-1} $hour^{-1}$ (BeneFusion VP1 Vet, Mindray, Germany) throughout the surgical procedure (Chohan and Davidow, 2017). Dexmedetomidine at a dose of 2 µg kg^{-1} intravenously (IV) was administered as premedication (Dexdomitor, Zoetis, Mexico). The depth of sedation was monitored using the scale established by Grint et al (2009). Anesthetic induction was performed using propofol (Recofol, Pisa, Mexico) at 3.5 mg Kg^{-1} (Branson, 2007). Once an adequate state of unconsciousness was achieved, orotracheal intubation was performed with connection to an anesthetic rebreathing circuit with an oxygen flow of 45 mL/ Kg^{-1} $minute^{-1}$. Anesthetic maintenance involved administering isoflurane (Sofloran, Pisa, Mexico) vaporized in oxygen at 100% while regulating the vaporizer's dial initially at 1.3% and then modifying the concentration according to the anesthetic depth required to maintain a mean arterial pressure (MAP) of 60-90 mmHg (Perkowski and Oyama, 2017). For surgical maintenance, the minimum alveolar concentration of isoflurane was maintained at 1.9 ± 0.19%, in addition to assessing jaw tone relaxation, ventromedial deviation of the eyeball, and absence of palpebral reflex. The dogs were ventilated mechanically, with the ventilator integrated into the anesthesia station (Wato-EX20 vet, Mindray, Germany), during the intraoperative period using a pressure-controlled ventilation method at a mean airway pressure (Paw) of 10-15 cmH_20 and a respiratory rate of 12 breaths per minute during surgery, as well as the maintenance of temperature between a range of 36 - 38 °C with the use of thermal support Equator® (EQ-5000, Smiths Medical ASD Inc., USA), evaluating body temperature using an esophageal thermometer within surgery events and in the post-operative period through rectal temperature. All surgeries were done by the same surgeon using a mid-line approach and a triple hemostatic surgical technique.

2.3. Experimental design

This study was conducted as a double-blind, prospective, randomized clinical trial. This was done by performing the surgical procedures without knowing the treatment. The researchers who conducted the evaluations and collected the results were unaware of the treatments and were not involved in selecting the animals or the data analysis. The investigator who performed the analyzes was unaware of the treatments.

Once all the animals were selected for the study, the IRT study variables and cardiovascular parameters were collected thirty minutes before administering anesthetic premedication with conscious animals, considering it the baseline event (E_{basal}). The instrumentation time had a mean duration of 35 ± 8 min. After this, the animals were induced into anesthesia in an average time of 45 ± 12 sec.

Once the anesthetic-surgical plane was reached, the dogs were medicated via epidurals in the lumbosacral space according to the assigned treatment group. The above was done twenty minutes before starting the surgery. The anesthetist used 22G-gauge Touhy-type epidural needles. The method was confirmed using the loss resistance technique (Valverde 2008; Hermeto et al 2017). Dogs were randomly assigned to three experimental groups: the lidocaine –control– group (GL, n = 7) medicated with 2 mg Kg^{-1}; the lidocaine-fentanyl group (GLF, n = 7) that received the same dose of lidocaine in combination with 3 µg Kg^{-1} of fentanyl; and the lidocaine-morphine group (GLM, n = 7) that received the same dose of lidocaine plus morphine at 0.1 mg Kg^{-1}. All groups received a volume of 0.1 ml kg^{-1}, with a final average volume of 0.74 ± 0.3 mL.

Once ensured continued surgical plane, the surgery was performed. The mean duration of the surgery was 30.7 ± 2.1 min., and anesthesia was 43.2 ± 1.7 min. The study variables were collected in the first incision (E_{Inc}), ligature and extraction of the right (E_{RoV}) and left ovarian pedicles (E_{LoV}), ligature and section of the cervix (E_{Ut}), reconstruction of the anatomical planes and skin suturing (E_{Sut}).

At the end of the surgery, recovery lasted 3.4 ± 1 min. Acute post-operative pain assessment was performed at 1 ($E_{1hr.}$), 2 ($E_{2hr.}$), and 3 ($E_{3hr.}$) hours after the surgery, using the DIVAS and UMPS pain assessment scale.

2.4. Infrared thermography

Thermographic images were obtained with an infrared camera (FLIR Thermal TM E80, FLIR Systems, USA). All images were collected with an emissivity of 0.95 and taken from the same side at a distance of 1 m. Thermographic images of the frontal region were taken to evaluate the upper left eyelid and lower left eyelid, ipsilateral tear gland in the left eye. The thermal images were visualized and analyzed with FLIR Tools software (FLIR Systems, USA). The regions of the upper left eyelid and lower left eyelid (thermographic window) were delimited manually in the software by a 4-cm line. Along this line, the high, average, and low-temperature readings were obtained in every study event. Concerning the tear gland, a thermographic point was marked at 1 mm from the medial commissure of the left eye to obtain the mean temperature of that region, as shown in Figures 1 and 2.

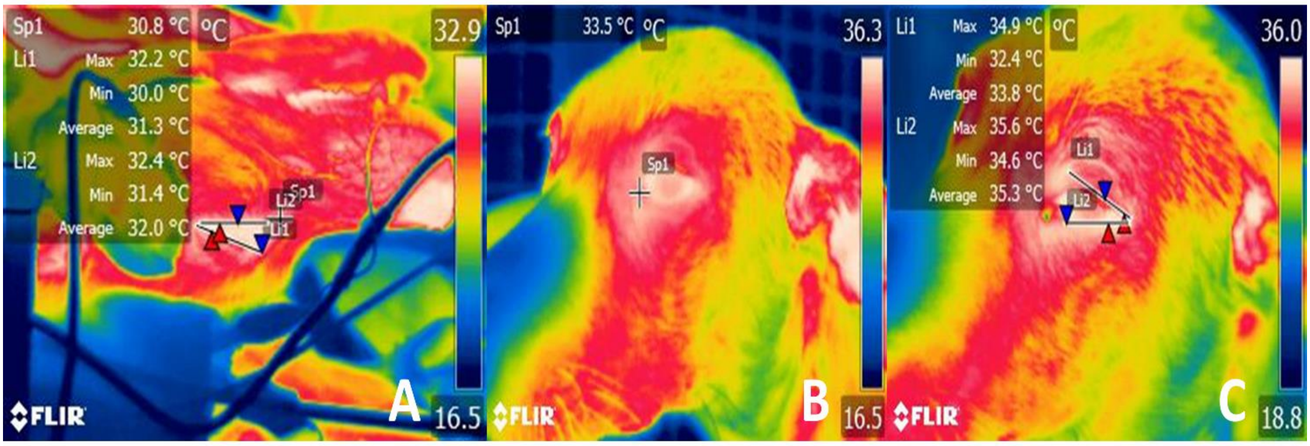

Figure 1 A. The region evaluated in the thermogram of the dogs during surgery was evaluated. A line was drawn for the Upper (Li1) and Lower Eyelid (Li2), and a focal point was fixed for the Tear Gland of the Left Eye (Sp1). The blue and red triangles indicate the low and high temperatures, respectively. B. Thermal region of the Tear Gland of the Left Eye, delimited by a focal point (Sp1) at approximately 1 mm from the medial commissure of the left eye. C. Thermal window of the Upper (Li1) and Lower Eyelid (Li2) delimited by a 4-cm line.

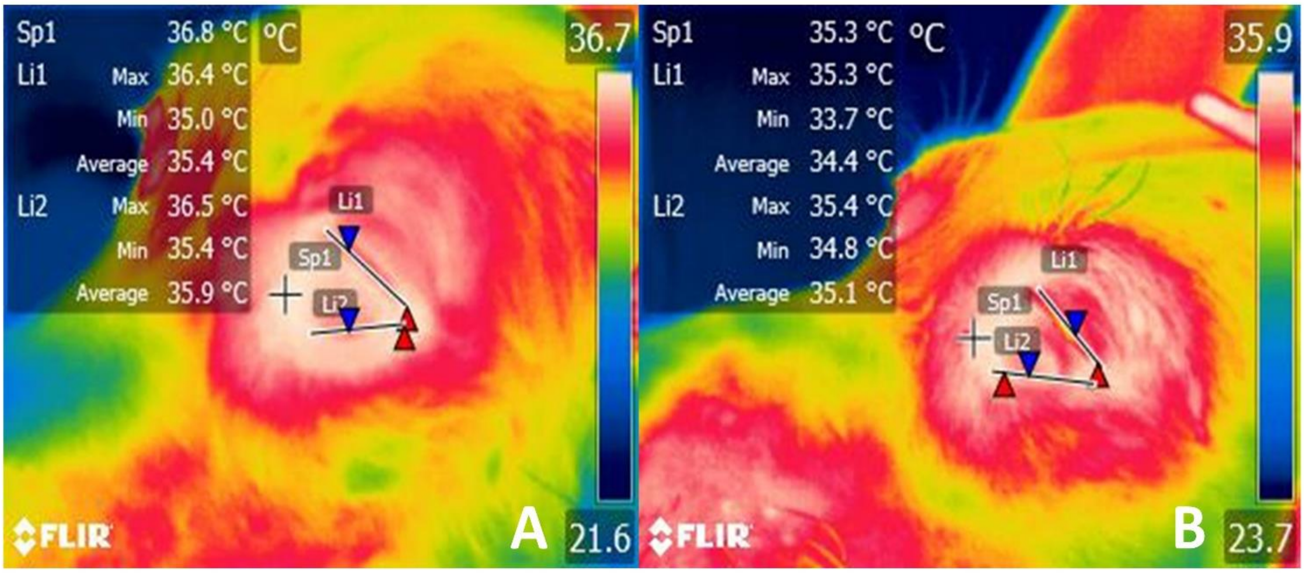

Figure 2 (A). Frontal region of a dog before the surgical stimulus, delimiting the thermal regions of the Upper (Li1) and Lower Eyelid (Li2), and the Tear Gland of the Left Eye (Sp1). The surface temperature of the latter (36.8°C) indicates that it was free of harmful stimuli. B. Frontal region of the same dog 1-hour post-surgery. The Tear Gland of the Left Eye presents a lower surface temperature of 1.5°C that was also detected in the Upper Eyelid. This could be attributed to the effect of the sympathetic stimulus caused by surgery and pain. The blue triangle indicates the low temperature and the red one indicates the high temperature.

2.5. Monitoring under anesthesia

2.5.1. Physiological parameters of the cardiorespiratory function

During the anesthetic-surgical procedure, the cardiorespiratory parameters were evaluated. Heart rate (HR) was measured through the electrocardiographic trace in the lead II, respiratory rate (RR) by spirometry, and non-invasive blood pressure (NIBP) by oscillometry in the radial artery at the level of the forearm region using a blood pressure cuff size # 3. Through this method, systolic blood pressure (SAP), mean arterial pressure (MAP), and diastolic blood pressure (DAP) were obtained. The esophageal temperature in degrees Celsius (°C) and pulse oximetry (SpO_2) were also monitored by infrared reading. Measurements were obtained through a multiparameter monitor (VS2000V, model UBEX, China). End-tidal CO_2 ($ETCO_2$) measurements were performed with the EMMA portable capnograph (Massimo, USA). The physiological parameters evaluated in the immediate post-operative period were HR, RR, and rectal temperature in °C.

2.6. Post-surgical pain evaluation

All evaluations were performed by the same previously-trained and qualified researcher. Two scales were used to evaluate post-surgical pain: DIVAS, where 0 mm reflects the absence of pain and 100 mm the maximum pain possible (Hernandez-Avalos et al 2019); and UMPS, which describes behavioral and physiological parameters, obtaining a maximum score of 27 points, interpreted as indescribable pain (Saberi Afshar et al 2017).

2.7. Analgesic rescue

If the subject of the study presented a minimum total score on the DIVAS scale ≤50 mm and a minimum UMPS score of 10, tramadol was administered at a dose of 3 mg Kg^{-1} IV (Pisadol, Pisa, Mexico) (Pascoe 2000). In the animals receiving rescue analgesia, the data collection continued.

2.8. Statistical analyses

Descriptive statistics were obtained for all the variables examined following the procedure outlined in the SAS statistical package (PROC MEANS) (SAS, 2012). Normality tests were done with Shapiro-Wilk normality tests (PROC UNIVARIATE, SAS 9.4) (SAS, 2012) for all the variables assessed in E_{basal} and for each perioperative event (E_{Inc}, E_{RoV}, E_{LoV}, E_{Ut}, E_{Sut}, $E_{1hr.}$, $E_{2hr.}$, $E_{3hr.}$) and treatment applied (analgesic epidural mixtures GL, GLF, GLM). A mixed linear model with a comparison of repeated means was used to evaluate the effect of the three epidural analgesic mixtures (treatments–T: GL, GLF, GLM) on the cardiorespiratory parameters, infrared thermographic images, and post-surgical pain evaluation scales.

The treatments and perioperative events were considered independent variables, while the cardiorespiratory parameters, thermographic values, and post-surgical pain scales were considered dependent variables. Interaction of treatment (T)*event (E) (SAS, 2012) was also performed. The mixed linear model included the fixed effects of the treatments (T), perioperative events (E), and first-order interactions between these factors and random effects on patients. The following statistical model was used for this purpose:

$$Yijk = \mu + \tau i + \tau j + \tau i \tau j + \beta k + eij$$

where:
Y = response variable (physiological biomarkers, infrared thermographic images, post-surgical pain scales)
τi = treatment effects (GL, GLF, GLM)
τj = perioperative events (E_{basal}, E_{Inc}, E_{RoV}, E_{LoV}, E_{Ut}, E_{Sut}, E_{1hr}, E_{2hr}, E_{3hr})
β = random effect (patient)
μ = population mean
e = residue

The PROC MIXED of the Statistical Analysis System (SAS 2012) was used to model the covariance structure. The variation between animals was specified using the RANDOM command, and covariance within the animals was specified using the REPEAT command. In all cases, the significance level was set at $P < 0.05$.

3. Results

In general, the duration of the motor block was 68.7 ± 9.6 min for GL, 98.4 ± 21.7 min for GLF, and 74.1 ± 13.1 min for GLM. No animal presented urinary retention in the post-operative period. Table 1 shows the thermography results of the eyelid and left tear gland of the bitches that underwent elective OVH. It reveals a statistically significant decrease in the surface temperature values of LELT in event E_{Inc} for GL (32.9°C±0.62), compared to GLF (34.2°C±0.62) and GLM (35.3°C±0.62) (P=0.006).

The infrared thermography response of eyelids in UEHT, UEMT, UELT, LEHT, and LEMT throughout the perioperative events do not display significant differences in GL and GLF ($P > 0.05$). Concerning LETG, observations show a statistically-significant increase ($P = 0.03$) in the infrared thermography of E_{basal} (36.8°C±0.63) and E_{Inc} (36.1°C±0.63) for GLM compared to the thermographic values for both the other perioperative events and groups.

In terms of the events for the same treatment, for GLM, we found that the infrared thermography values decreased progressively and significantly from E_{OvD} up to E_{3hr} in UELT (E_{RoV} 35.3°C±0.55; E_{3hr} 35.0°C±0.55) ($P = 0.02$), LEHT (E_{RoV} 35.5°C±0.58; E_{3hr} 35.2°C±0.58) ($P = 0.03$), LEMT (E_{RoV} 34.9°C±0.58; E_{3hr} 34.8°C±0.58) ($P = 0.03$), and LELT (E_{RoV} 34.3°C±0.62; E_{3hr} 34.0°C±0.62) ($P = 0.01$). However, a significant decrease in the infrared thermography value of the post-surgical period was observed only in UEMT (E_{1hr} 33.9°C±0.64; E_{2hr} 33.8°C±0.64), E_{3hr} (33.4°C±0.64) ($P = 0.01$), and UELT (E_{1hr}, 32.7°C±0.69 E_{2hr} 32.6°C±0.69 and E_{3hr} 31.7°C±0.69) ($P = 0.006$).

To LETG, we observed a progressive decrease in the infrared thermographic surface response between events in the same treatment with statistically-significant differences from E_{RoV} (35.2°C±0.63) ($P = 0.02$) up to the final evaluation at E_{3hr} (35.3°C±0.63) ($P < 0.01$) for GLM.

3.1. Physiological parameters

Table 2 presents the results for the cardiorespiratory parameters of the dogs subjected to elective OVH. No significant differences were observed for HR in any treatment (GL, GLF, GLM) or among the perioperative events.

Regarding body temperature (T°C), treatments GL and GLF presented significant decreases in temperature values compared to GLM ($P = 0.02$). However, the results for events E_{LoV} and E_{Ut} in GL and GLF showed lower temperatures than GLM ($P = 0.02$). Meanwhile, for E_{Inc}, the GL treatment showed a significant decrease in body temperature compared to GLF and GLM ($P = 0.02$). The intraoperative events in general (E_{Inc} to E_{Sut}) showed a gradual reduction in body temperature in all three treatment groups (GLM, GLF, GL) ($P = 0.01$). The values for the post-surgical events (E_{1hr}, $E_{2hr,}$ and E_{3hr}) did not present any significant differences with respect to the values for E_{basal}.

The variables SAP, DAP, and MAP showed no significant differences among treatments, but the dogs in GL did show significant differences ($P = 0.01$) during events $E_{Inc.}$ and E_{Sut} concerning E_{basal}.

Table 1 Effect of three different epidural blocks (T) and perioperative events (E) on the infrared thermography of the frontal region (Mean ± Standart Error, SE) in bitches undergoing elective OVH.

Region assessed	Treatments	Perioperative event (mean ± SE)									*P*-value	Interaction T*E
		E_{basal}	$E_{Inc.}$	E_{RoV}	E_{LoV}	E_{Ut}	E_{Sut}	$E_{1 hr.}$	$E_{2 hr.}$	$E_{3 hr.}$		
UEHT	GL	35.9^{a,1}	35.2^{a,1}	35.8^{a,1}	35.6^{a,1}	34.6^{a,1}	35.4^{a,1}	35.6^{a,1}	34.7^{a,1}	35.0^{a,1}	p=0.87	p=0.76
(T °C)	n=7	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55		
	GLF	35.6^{a,1}	35.4^{a,1}	35.4^{a,1}	36.0^{a,1}	35.0^{a,1}	34.6^{a,1}	34.9^{a,1}	36.1^{a,1}	35.3^{a,1}	p=0.46	
	n=7	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55		
	GLM	36.7^{a,1}	36.3^{a,b,1}	35.3^{a,b,1}	35.5^{a,b,1}	35.4^{a,b,1}	35.4^{a,b,1}	35.1^{b,1}	34.9^{b,1}	35.0^{b,1}	p=0.02	
	n=7	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55	±0.55		
	P-value	p=0.28	p=0.34	p=0.53	p=0.63	p=0.35	p=1.00	p=0.56	p=0.12	p=0.70		
UEMT	GL	34.4^{a,1}	34.7^{a,1}	34.7^{a,1}	34.7^{a,1}	34.7^{a,1}	34.7^{a,1}	34.7^{a,1}	33.5^{a,1}	34.6^{a,1}	p=0.33	p=0.96
(T °C)	n=7	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64		
	GLF	34.6^{a,1}	34. ^{a,1}	34.6^{a,1}	34.6^{a,1}	34.6^{a,1}	34.6^{a,1}	34.0^{a,1}	34.1^{a,1}	34.6^{a,1}	p=0.47	
	n=7	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64	±0.64		
	GLM	35.6^{a,1}	35.3^{a,1}	35.3^{a,1}	35.3^{a,1}	35.3^{a,1}	35.3^{a,1}	33.9^{a,b,1}	33.8^{a,b,1}	33.4^{b,1}	p=0.01	
	n=7	±0.64	±0.64	±0.64	±0.64	±0.55	±0.64	±0.64	±0.64	±0.64		
	P-value	p=0.31	p=0.50	p=0.50	p=0.50	p=0.50	p=0.50	p=0.45	p=0.75	p=0.74		
UELT	GL	33.5^{a,b,1}	33.7^{a,b,1}	32.5^{a,b,1}	34.0^{a,1}	32.9^{a,b,1}	32.0^{b,1}	33.8^{a,b,1}	32.5^{a,b,1}	32.9^{a,b,1}	p=0.04	p=0.67
(T °C)	n=7	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69		
	GLF	33.8^{a,1}	33.7^{a,1}	33.7^{a,1}	33.5^{a,1}	33.1^{a,1}	33.0^{a,1}	32.8^{a,1}	32.9^{a,1}	33.3^{a,1}	p=0.31	
	n=7	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69		
	GLM	34.4^{a,1}	34.1^{a,1}	33.9^{a,1}	33.6^{a,1}	33.6^{a,1}	33.5^{a,b,1}	32.7^{a,b,1}	32.6^{a,b,1}	31.7^{a,1}	p=0.006	
	n=7	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69	±0.69		
	P-value	p=0.53	p=0.67	p=0.87	p=0.70	p=0.59	p=0.62	p=0.31	p=0.74	p=0.69		
LEHT	GL	35.9^{a,1}	35.3^{a,1}	35.5^{a,1}	35.8^{a,1}	35.0^{a,1}	34.8^{a,1}	35.7^{a,1}	35.3^{a,1}	35.6^{a,1}	p=0.44	p=0.40
(T °C)	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	GLF	36.0^{a,1}	35.5^{a,1}	35.1^{a,1}	35.0^{a,1}	35.2^{a,1}	34.8^{a,1}	35.7^{a,1}	35.3^{a,1}	35.8^{a,1}	p=0.76	
	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	GLM	37.2^{a,1}	36.3^{a,b,1}	35.5^{b,1}	35.4^{b,1}	35.2^{b,1}	34.9^{b,1}	35.2^{b,1}	35.5^{b,1}	35.2^{b,1}	p=0.005	
	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	P-value	p=0.35	p=0.33	p=0.98	p=0.61	p=0.97	p=0.97	p=0.97	p=0.78	p=0.80		
LEMT	GL	35.3^{a,1}	34.1^{a,1}	34.9^{a,1}	35.0^{a,1}	34.2^{a,1}	33.7^{a,1}	35.6^{a,1}	34.5^{a,1}	34.8^{a,1}	p=0.76	p=0.64
(T °C)	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	GLF	35.1^{a,1}	35.2^{a,1}	34.8^{a,1}	34.3^{a,1}	34.5^{a,1}	34.2^{a,1}	35.2^{a,1}	34.6^{a,1}	35.2^{a,1}	p=1.00	
	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	GLM	36.7^{a,1}	35.8^{a,b,1}	34.9^{b,c,1}	34.9^{b,c,1}	34.7^{b,c,1}	34.2^{c,1}	34.8^{b,c,1}	35.0^{b,c,1}	34.8^{b,c,1}	p=0.002	
	n=7	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58	±0.58		
	P-value	p=0.05	p=0.05	p=0.89	p=0.81	p=0.76	p=0.94	p=0.65	p=0.61	p=0.90		
LELT	GL	34.7^{a,1}	32.9^{a,2}	33.9^{a,1}	34.6^{a,1}	33.7f,^{a,1}	33.3^{a,1}	34.9^{a,1}	34.3^{a,1}	34.0^{a,1}	p=0.84	p= 0.73
(T °C)	n=7	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62		
	GLF	34.7^{a,1}	34.2^{a,1,2}	34.4^{a,1}	34.0^{a,1}	33.6^{a,1}	33.6^{a,1}	34.5^{a,1}	33.8^{a,1}	34.3^{a,1}	p=0.83	
	n=7	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62		
	GLM	36.2^{a,1}	35.3^{a,b,1}	34.3^{b,c,1}	34.3^{b,c,1}	34.2^{b,c,1}	33.4^{c,1}	34.1^{b,c,1}	34.3^{b,c,1}	34.0^{b,c,1}	p=0.002	
	n=7	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62	±0.62		
	P-value	p=0.09	p=0.006	p=0.62	p=0.78	p=0.59	p=0.82	p=0.66	p=1.00	p=0.74		
LETG	GL	35.2^{a,1}	34.3^{a,1,2}	34.2^{a,1}	34.3^{a,1}	33.6^{a,1}	33.5^{a,1}	34.2^{a,1}	35.0^{a,1}	34.5^{a,1}	p=0.81	p= 0.36
(T °C)	n=7	±0.63	±0.3	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63		
	GLF	34.7^{a,1}	34.2^{a,2}	34.6^{a,1}	34.1^{a,1}	34.1^{a,1}	33.7^{a,1}	34.5^{a,1}	34.9^{a,1}	35.0^{a,1}	p=0.94	
	n=7	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63		
	GLM	36.8^{a,1}	36.1^{a,b,1}	35.2^{a,b,1}	35.3^{a,b,1}	35.0^{a,b,1}	34.7^{b,1}	35.1^{a,b,1}	35.2^{a,b,1}	35.3^{a,b,1}	p=0.02	
	n=7	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63	±0.63		
	P-value	p=0.08	p=0.005	p=0.52	p=0.28	p=0.31	p=0.29	p=0.49	p=0.83	p=0.73		

a,b,c: different literals by row indicate significant differences between events for the same treatment
1,2,3: different numerals by column indicate significant differences between treatments for the same event
T= treatments (GL: lidocaine group; GLF: lidocaine-fentanyl group; GLM: lidocaine-morphine group)
E: perioperative event (E_{basal}: 30 min. pre-surgical; E_{Inc}: incision; E_{RoV}: right ovarian ligation; E_{LoV}: left ovarian ligation; E_{Ut}: uterine ligation; E_{Sut}: suture; $E_{1hr.}$: 1 hour post-surgery; $E_{2hr.}$: 2 hours post-surgery; $E_{3hr.}$: 3 hours post-surgery
UEHT: upper eyelid high temperature; UEMT: upper eyelid medium temperature; UELT: upper eyelid low temperature; LEHT: lower eyelid high temperature; LEMT: lower eyelid medium temperature; LELT: lower eyelid low temperature; LETG: left eye tear gland.

3.2. Post-surgical pain evaluation scales

Table 3 presents the results of the DIVAS and UMPS post-surgical pain evaluation scales. No significant differences occurred among treatments (*P* > 0.05) or post-surgical events (*P* > 0.05). 2 animals received analgesic rescue, one present in GL and one in GLF. No significant difference was determined for T*E interaction for any of the variables analyzed (*P* > 0.05).

4. Discussion

4.1. Infrared thermography

The present study results supported the hypothesis that administering lidocaine alone or combined with morphine and fentanyl would prevent changes in infrared thermographic response and cardiorespiratory parameters associated with nociception and perioperative pain in bitches under OVH elective. The results showed that the IRT response in the eyelids was similar for UEHT, UEMT, LEHT, and LEMT, with no statistically significant differences between the three epidural treatments used (P> 0.05). These findings reveal the perioperative analgesic effect of the epidural protocol in modulating the sympathetic response. The above is consistent with what Hernández-Avalos et al (2021) expressed, who mentioned that using analgesics during a surgical procedure prevents and reduces autonomic reflexes derived from nociception. Similarly, Mansour et al (2020) describe poor pain management and control results in sympathetic stimulation known as autonomic hemodynamic reactivity.

The IRT assesses changes in the surface temperature that are influenced by the blood flow of the superficial capillaries, controlled by the activity of the ANS. When there is a decrease in temperature at the thermal window of the lacrimal caruncle, this phenomenon can be associated with stimulating the sympathetic nervous system and the neurosecretion of catecholamines, causing vasoconstriction of capillaries (Casas-Alvarado et al 2020). Lush and Ichiji (2018) evaluated dogs undergoing orchiectomy and obtained a moderately positive correlation (r^2 = 0.48) between the surface temperature of the tear caruncle and the University of Glasgow's pain evaluation scale. In contrast, a study by Saeki et al (2021) observed that the temperature of the nasal region increased by 4.4 ºC without observing changes in the behavior associated with pain in dogs under radiation therapy for the treatment of nasal tumors. This data shows divergent information because the activation of the ANS results in a hyperthermic phenomenon associated with stress during pain perception (Mota Rojas et al 2021). This has been observed in a study where the eye temperature level increased to 2 ºC in dogs presenting psychogenic stress due to separation from the owner (Travain et al 2015). These observations suggest the need of more regarding the usefulness of this anatomical region to detect changes associated with the perception of pain in dogs.

In other species, such as cattle, the stimulation of ANS during nociception is associated with a decrease in surface temperature in the thermal windows of the lacrimal caruncle due to peripheral vasoconstriction produced by the neurosecretion of catecholamines (Stewart et al 2008, 2009, 2010). However, Readelli et al (2019) mention that this thermal response can be attenuated with analgesics. Drugs like lidocaine decrease the sympathetic vasomotor response due to the blockade of sympathetic fibers (Fischer and Pinnock, 2004) responsible for transmitting the nociceptive impulse (Lamont 2008; Hernandez-Avalos et al 2019). This effect can be potentiated when administered with other drugs, including opioids (Arora et al 2015; Steagall 2017). Therefore, in the present study, the administration of lidocaine alone or combined with pure opioids prevented changes in the recorded IRT values, where the study animals manifested prolonged perioperative analgesia. However, it is necessary to consider that in the present study, the dogs have been sedated with α-2-adrenergic agonists, such as dexmedetomidine, which initially produces a vasoconstriction effect and can alter the radiation response early (Vainionpää et al 2013). Although this physiological response is related to the half-life of dexmedetomidine (about 36 min when administered IV), as reported and correlated in pharmacokinetic analyzes (Dent et al 2019). In the present study, the instrumentation time was 35 ± 8 min, so this vasoconstriction effect was not observed during the anesthetic-surgical procedure, where bitches showed hemodynamic stability and normal MAP values for anesthetized patients.

For GLM during the evaluation of LEHT and UEHT, as well as LEMT and LELT, a progressive decrease in surface temperatures from E_{OvD} to the final reading at E_{3hr} was observed. This may be due to the direct effect of the opioid that, in combination with inhaled anesthetics, alters thermoregulation thresholds, causing a continuous temperature decrease (Morrison and Nakamura, 2011). These conditions can induce a heat exchange effect counter-current to the blood that arrives at the vascular beds of the skin, which lose temperature to the environment (Robinson, 2014).

This work contributes to veterinary medicine because it demonstrates the feasibility of using IRT of the eyelids and tear glands to evaluate pain in animals. However, we suggest assessing additional anatomical regions during other surgical procedures to correlate the results with other available methods to evaluate the autonomous hemodynamic reactivity associated with nociceptive stimuli to continue validating thermography as a non-invasive method for assessing nociception.

A limitation of this study is the use of thermal support to avoid severe hypothermia in animals under anesthesia. This could have influenced the IRT readings by emitting more radiation or hot wind from the thermal support equipment (Aarnes et al 2017). Similar to that reported in larger species where wind altered the IRT reading (Mota-Rojas et al 2021).

4.2. Cardiorespiratory parameters

The intraoperative monitoring of the cardiovascular function did not show significant differences within the treatments -GL, GLF, GLM- (P > 0.05). This may be because the epidural administration of lidocaine, in combination with the MAC of the inhalation anesthetic used in this study, was necessary to attenuate the nociceptive response during surgery and the immediate post-operative period (Johnson, 2016). This is also enhanced with pure opioids such as morphine and fentanyl, whose analgesic effect depends on their binding to μ receptors in the A-δ fibers, blocking the upward transmission of the nociceptive stimulus (Valverde, 2008).

Concerning temperature, statistically significant differences were observed (P < 0.05) in treatments GL and

GLF. The explanation for this phenomenon can be attributed to two effects. Firstly, dexmedetomidine causes peripheral vasoconstriction due to the agonism of the α_2-adrenergic receptors that cause the retention of the central temperature, although its impact is brief (Dent et al 2019). With the elimination of this drug, a predominance of vasodilation caused by the combination of inhalation anesthetic, lidocaine, and opioids is observed, blocking the sympathetic postganglionic fibers and promoting heat loss (Morrison et al 2008; Bruells and Rossaint 2011). Adding cold substances such as antiseptics and celiotomy in haircutting contributes to heat loss due to thermal exchange with the environment (Robinson 2014).

Table 2 Effect of three different epidural blocks (T) and perioperative events (E), on the cardiorespiratory parameters (Mean ± Standar Error, SE) of bitches undergoing elective OVH.

Cardiorespiratory parameters	Treatments	Perioperative event (mean ± SE)									*P*-value	Interaction T*E
		E_{basal}	$E_{Inc.}$	E_{RoV}	E_{LoV}	E_{Ut}	E_{Sut}	$E_{1\ hr.}$	$E_{2\ hr.}$	$E_{3\ hr.}$		
HR	GL	$105^{a,1}$	$119^{a,1}$	$103^{a,1}$	$112^{a,1}$	$106^{a,1}$	$110^{a,1}$	$114^{a,1}$	$108^{a,1}$	$108^{a,1}$	p=0.64	p=0.47
(bpm)	n=7	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54		
	GLF	$107^{a,1}$	$105^{a,1}$	$103^{a,1}$	$102^{a,1}$	$117^{a,1}$	$110^{a,1}$	$103^{a,1}$	$108^{a,1}$	$110^{a,1}$	p=0.52	
	n=7	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54		
	GLM	$107^{a,1}$	$120^{a,1}$	$107^{a,1}$	$106^{a,1}$	$100^{a,1}$	$103^{a,1}$	$108^{a,1}$	$101^{a,1}$	$110^{a,1}$	p=0.39	
	n=7	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54	±7.54		
	P-value	p=0.85	p=0.95	p=0.76	p=0.60	p=0.13	p=1.00	p=0.54	p=0.93	p=0.94		
RR	GL	$23^{a,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$23^{a,2}$	$23^{a,2}$	$22^{a,1}$	p=0.0001	p=0.46
(bpm)	n=7	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86		
	GLF	$24^{a,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$9^{b,1}$	$20^{a,2}$	$22^{a,2}$	$24^{a,1}$	p=0.0001	
	n=7	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86		
	GLM	$29^{a,1}$	$11^{c,1}$	$10^{c,1}$	$12^{c,1}$	$10^{c,1}$	$11^{c,1}$	$30^{a,1}$	$29^{a,1}$	$23^{b,1}$	p=0.0001	
	n=7	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86	±1.86		
	P-value	p=0.05	p=0.58	p=0.78	p=0.21	p=0.66	p=0.58	p=0.004	p=0.03	p=0.70		
T (°C)	GL	$38.0^{a,1}$	$36.5^{b,2}$	$36.1^{b,c,1}$	$36.0^{b,c,2}$	$35.^{b,c,2}$	$35.2^{c,1}$	$37.3^{a,1}$	$38.1^{a,1}$	$37.7^{a,1}$	p=0.0003	p=0.88
	n=7	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38		
	GLF	$38.1^{a,1}$	$37.8^{a,b,c,1}$	$36.7^{c,d,1}$	$36.8^{c,d,1,2}$	$36.4^{c,d,1,2}$	$35.8^{c,1}$	$37.1^{a,b,c,d,1}$	$38.0^{a,b,1}$	$38.0^{a,b,c,1}$	p=0.007	
	n=7	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38		
	GLM	$38.6^{a,1}$	$37.5^{a,b,1,2}$	$37.1^{b,1}$	$37.2^{b,1}$	$37.0^{b,1}$	$35.7^{c,1}$	$37.6^{a,b,1}$	$37.9^{a,b,1}$	$38.0^{a,b,1}$	p=0.006	
	n=7	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38	±0.38		
	P-value	p=0.41	p=0.02	p=0.45	p=0.02	p=0.02	p=0.31	p=0.59	p=0.95	p=0.93		
SAP	GL	$124^{a,1}$	$92^{b,1}$	$96^{a,b,1}$	$104^{a,b,1}$	$93^{b,1}$	$89^{b,1}$	*	*	*	p=0.001	p=0.20
(mmHg)	n=7	±7.52	±7.52	±7.52	±7.52	±7.52	±7.52					
	GLF	$95^{a,1}$	$93^{a,1}$	$102a^{,1}$	$105a^{,1}$	$90^{a,1}$	$92^{a,1}$	*	*	*	p=0.14	
	n=7	±7.52	±7.52	±7.52	±7.52	±7.52	±7.52					
	GLM	$91^{a,1}$	$105^{a,1}$	$101^{a,1}$	$100^{a,1}$	$96^{a,1}$	$91^{a,1}$	*	*	*	p=0.17	
	n=7	±7.52	±7.52	±7.52	±7.52	±7.52	±7.52					
	P-value	p=0.08	p=0.25	p=0.90	p=0.89	p=0.55	p=0.92					
MAP	GL	$93^{a,1}$	$68^{b,c,1}$	$70^{b,c,1}$	$79^{a,b,1}$	$71^{b,c,1}$	$59^{c,1}$	*	*	*	p=0.0007	p=0.15
(mmHg)	n=7	±6.90	±6.90	±6.90	±6.90	±6.90	±6.90					
	GLF	$65^{a,1}$	$69^{a,1}$	$80^{a,1}$	$76^{a,1}$	$65^{a,1}$	$67^{a,1}$	*	*	*	p=0.11	
	n=7	±6.90	±6.90	±6.90	±6.90	±6.90	±6.90					
	GLM	$61^{a,1}$	$76^{a,1}$	$77^{a,1}$	$79^{a,1}$	$70^{a,1}$	$62^{a,1}$	*	*	*	p=0.07	
	n=7	±6.90	±6.90	±6.90	±6.90	±6.90	±6.90					
	P-value	p=0.05	p=0.38	p=0.69	p=1.00	p=0.63	p=0.40					
DAP	GL	$77a^{,1}$	$56^{b,c,1}$	$58a^{,bc,1}$	$67a^{,b,1}$	$60a^{,b,c,1}$	$47^{c,1}$	*	*	*	p=0.003	p= 0.35
(mmHg)	n=7	±7.02	±7.02	±7.02	±7.02	±7.02	±7.02					
	GLF	$50^{a,1}$	$57^{a,1}$	$62^{a,1}$	$61^{a,1}$	$51^{a,1}$	$54^{a,1}$	*	*	*	p=0.20	
	n=7	±7.02	±7.02	±7.02	±7.02	±7.02	±7.02					
	GLM	$49^{a,1}$	$61^{a,1}$	$64^{a,1}$	$66^{a,1}$	$57^{a,1}$	$51^{a,1}$	*	*	*	p=0.09	
	n=7	±7.02	±7.02	±7.02	±7.02	±7.02	±7.02					
	P-value	p=0.006	p=0.64	p=0.87	p=0.94	p=0.80	p=0.48					
$ETCO_2$	GL	$31^{a,1}$	$33^{a,1}$	$30^{a,2}$	$30^{a,2}$	$29^{a,2}$	$31^{a,1}$	*	*	*	p=0.10	p= 0.40
(mmHg)	n=7	±1.54	±1.54	±1.54	±1.54	±1.54	±1.54					
	GLF	$32^{a,1}$	$35^{a,1}$	$34^{a,1}$	$35^{a,1}$	$34^{a,1}$	$34^{a,1}$	*	*	*	p=0.19	
	n=7	±1.54	±1.54	±1.54	±1.54	±1.54	±1.54					
	GLM	$31^{a,1}$	$35^{a,1}$	$32^{a,1,2}$	$33^{a,1,2}$	$34^{a,1,2}$	$32^{a,1}$	*	*	*	p=0.13	
	n=7	±1.54	±1.54	±1.54	±1.54	±1.54	±1.54					
	P-value	p=0.55	p=0.94	p=0.03	p=0.02	p=0.02	p=0.10					
SpO_2	GL	96	98	97	98	96	98	*	*	*	p=0.66	p=0.28
(%)	n=7	± 0.67	± 0.75	± 0.30	± 0.42	± 1.7	± 0.36					
	GLF	95	98	98	98	98	98	*	*	*	p=0.12	
	n=7	± 1.87	± 0.68	± 0.63	± 0.48	± 0.75	± 0.48					
	GLM	97	97	96	96	97	98	*	*	*	p=0.40	
	n=7	± 0.59	± 0.78	± 1.06	± 0.97	± 0.75	± 0.98					
	P-value	p=0.66	p=125	p=0.66	p=0.91	p=0.23	p=0.28					

a,b,c,d: different literals by row indicate significant differences between events for the same treatment
1,2,3: different numerals by column indicate significant differences between treatments for the same event
T= treatments (GL: lidocaine group; GLF: lidocaine-fentanyl group; GLM: lidocaine-morphine group)

E: perioperative event (E_{basal}: 30 min. pre-surgical; E_{Inc}: incision; E_{RoV}: right ovarian ligation; E_{LoV}: left ovarian ligation; E_{Ut}: uterine ligation; E_{Sut}: suture; $E_{1hr.}$: 1 hour post-surgery; $E_{2hr.}$: 2 hours post-surgery; $E_{3hr.}$: 3 hours post-surgery
HR= heart rate; RR= respiratory rate; T= temperature (during events basal, 1 hr, 2 hr y 3 hr. rectal temperature was obtained, whilemientras at events $E_{Inc,}$ E_{RoV}; E_{LoV}; E_{Ut}; E_{Sut} esophageal reading was performed) SAP= systolic blood pressure; MAP= mean arterial pressure; DAP= diastolic arterial pressure; $ETCO_2$= End- Tidal CO_2
*Not determined by divice disposition.

The mentioned findings show no significant changes in the cardiorespiratory parameters evaluated during the study. Therefore, it can be accepted that lidocaine alone or in combination with opioids avoided the cardiovascular changes associated with nociception. The effect of inhaled anesthetics, causing central depression, and avoiding the autonomic reflex to a nociceptive stimulus are also elements that need to be considered. However, a limitation of this study is the lack of knowledge of the exact amount of anesthetic expired in the animals.

4.3. Post-surgical pain evaluation scales

The DIVAS and UMPS scales demonstrated that the analgesic effect and efficacy seen during the post-surgical events ($E_{1hr.}$, $E_{2hr.}$ and $E_{3hr.}$) were similar among the patients in the study. Similarly, Abelson et al (2011) reported no significant differences after administering morphine alone or in combination with local analgesics. In contrast, the use of opioids has been associated with lower scores on post-operative pain scales, suggesting a greater analgesic effect (Tusell et al 2005; Bosmans et al 2012; Steagall 2017). When local analgesics are used in conjunction with opioids, the analgesic effect of medications is potentiated by inhibiting the transduction of the nociceptive stimulus and its transmission (Lamont, 2008). Hence, the evaluation of pain during the immediate post-operative period allows recognition of the animal's behavior during the long-term post-operative recovery (Saberi Afshar et al 2017), according to some research, the combination of local analgesics with pure opioids manages to control pain (Garcia-Pereira 2018; Steagall 2017). In previous studies, it has been reported that if the pain is effectively controlled, the clinical signs associated with this sign are minimal or null during the immediate post-operative period. For example, Fazio et al (2015) observed that both the behavioral and hematological changes associated with pain did not occur during the immediate post-operative period, which is indicative for these authors of antinociceptive efficacy during surgery, similar to that observed in some studies (Morgaz et al 2013; Berry 2015). For this reason, if no changes are observed during the immediate post-operative period, the analgesic requirements are reduced in this period, in addition to the fact that if the scores obtained by structured scales to assess behavior remain low, the frequency of subsequent evaluation can be extended in the interval.

Table 3 Effect of three different epidural blocks (T) and post-surgical events (E), on the post-surgical pain evaluation scales (Mean ± Standard Error, SE) in bitches undergoing elective OVH.

Pain evaluation scales	Treatments	Post-surgical events (mean ± SE)			*P*-value	Interaction T*E
		$E_{1hr.}$	$E_{2hr.}$	$E_{3hr.}$		
DIVAS	GL n=7	$28^{a,1}$ ±7	$32^{a,1}$ ±7	$31^{a,1}$ ±7	p=0.88	p=0.35
	GLF n=7	$25^{a,1}$ ±7	$21^{a,1}$ ±7	$12^{a,1}$ ±7	p=0.66	
	GLM n=7	$30^{a,1}$ ±7	$25^{a,1}$ ±7	$24^{a,1}$ ±7	p=0.66	
	P-value	p=0.88	p=0.47	p=0.06		
UMPS	GL n=7	$4^{a,1}$ ±0.7	$3^{a,1}$ ±0.7	$4^{a,1}$ ±0.7	p=0.61	p=0.11
	GLF n=7	^{a,1} ±0.7	$3^{a,1}$ ±0.7	$3^{b,1}$ ±0.7	p=0.31	
	GLM n=7	$4^{a,1}$ ±0.7	$4^{a,1}$ ±0.7	$4^{a,1}$ ±0.7	p=0.77	
	P-value	p=0.66	p=0.56	p=0.88		

a,b,c different literals by row indicate significant differences between events for the same treatment
1,2,3 different numerals by column indicate significant differences between treatments for the same event
T= treatments (GL: lidocaine group; GLF: lidocaine-fentanyl group; GLM: lidocaine-morphine group)
E: post-surgical event ($E_{1hr.}$: 1 hour post-surgery; $E_{2hr.}$: 2 hours post-surgery; $E_{3hr.}$: 3 hours post-surgery)
DIVAS: Dynamic Interactive Visual Analogous Scale
UMPS: University of Melbourne Pain Scale.

On the other hand, Giannoudis et al (2006) describe that increases in heart rate and blood pressure can reach 20%, compared to baseline values. In the present study. This effect was not reported in the present study due to the hemodynamic stability evaluated and recorded during the perioperative period. These findings are similar to reports on human patients, where pain monitoring is based on observing autonomic reactions derived from nociception indices, in which a negative relationship between hemodynamic reactivity and pain assessments has been suggested (Boselli et al 2013). However, because of the significant influence that evaluations of IRT could have concerning autonomic hemodynamic reactivity, both tools could share a similar correlation to the one observed in human medicine but with even greater sensitivity.

An explanation of the absence of alterations in microcirculation is due to analgesics that prevented autonomic hemodynamic reactivity, as is supported by the autonomic reaction with the thermographic indicators that, especially in this study, show a possible relation with pain that has been seen in other species (Redaelli et al 2019). In this regard, upon comparing the thermographic biomarkers from the left eye with the pain scores, we found that they coincide with the absence of significant differences ($P > 0.05$).

The presence of two animals that required analgesic rescue differed from that reported by other authors. They mention that less analgesia was provided in the groups where monotherapy drugs were used than in the combination of two analgesics (Garcia-Pereira 2018). Tramadol, used in rescue analgesic, is a drug with a serotonergic activity that provides similar analgesia to that reported when administering pure opioids during surgical procedures such as OVH in bitches (Mastrocinque and Fantoni 2003; Zhang et al 2017; Oliva- Domínguez et al 2021). In this sense, in some studies, they observed that in the animals requiring analgesic rescue, tramadol proved effective for controlling acute pain in dogs despite having received non-steroidal analgesics prior to surgery (Imagawa et al 2011; Teixeira et al 2013). In this work, combining pure opioids with lidocaine did not produce any advantage in preventing nociception, which could be corroborated by the similar scores obtained in the pain assessment scales. A possible limitation of this study is that the methods used to corroborate the correct administration of epidural drugs have been identified as insufficient (Adami and Gendron 2017). Some authors suggest that superior efficacy is obtained in a regional block with ultrasound-guided or electrostimulation methods (Iff et al 2007; Otero et al 2014; Elsharkawy et al 2017). Although the efficacy of the treatments used is corroborated, this could have influenced the effectiveness of the treatments.

The scientific data consulted demonstrate that the use of epidural lidocaine provides analgesia with a duration of 60-120 minutes (Jones 2001; Gomez de Segura et al 2009), which differs from our observations in this experiment, where the pain scales indicated that immediate post-operative analgesia lasted for 3h. Additionally, when the lidocaine is administered in combination with pure opioids like fentanyl or morphine, the analgesia provided can last up to 24h (Garcia-Pereira 2018).

Finally, the motor block duration was 68.7 ± 9.6 min for GL, 98.4 ± 21.7 min for GLF, and 74.1 ± 13.1 min for GLM. This differs from what was reported in review studies where they indicate that the combination of opioids with local analgesics provides a shorter motor block than the single use of these drugs (Steagall 2017; Wendt-Hornickle and Snyder 2016). A possible explanation for this event could be that being both the lidocaine and the opioid drugs lipophilic, which could increase the time of blockade on the motor fibers (Garcia-Pereira 2018; Valverde 2008). Therefore, a smaller amount may be required to avoid it, although more studies are needed to corroborate this fact.

5. Conclusions

It is accepted that the hypothesis use of lidocaine with morphine or fentanyl prevented the changes in IRT and cardiovascular response associated with nociception. These findings were clinically correlated to the DIVAS and UMPS acute pain assessment scale scores during the immediate post-operative period of bitches subjected to elective ovariohysterectomy.

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Ethical considerations

The experimental protocol was approved (Code number CAMCA.05.19) by the Scientific Commission of the Master in Science (CAMCA) "Maestría en Ciencias Agropecuarias" of the Faculty of Veterinary Medicine and Animal Husbandry, Universidad Autónoma Metropolitana, Mexico City, Mexico. The procedures for handling the animals while drawing blood samples met the requirements established in the Official Mexican Norm NOM-062-ZOO-1999: "Specifications and techniques for the production, care, and use of laboratory animals". The experiment was conducted strictly following instructions for the ethical use of animals (Sherwin et al 2003). During surgery or the taking of infrared thermographic images, no phase of the study resulted in any animal being injured, mutilated, or overhandled. No animal died during or after surgery, and it was not necessary to euthanize any patient.

Conflict of Interest

The authors declare that there is no conflict of interest with this work.

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