RESEARCH PAPER

Preperitoneal ropivacaine infusion *versus* epidural ropivacaine–morphine for postoperative analgesia in dogs undergoing ovariohysterectomy: a randomized clinical trial

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Abstract

Objective To assess the effect of continuous wound infusion (CWI) with preperitoneal ropivacaine on postoperative analgesia and compare it with the epidural administration of ropivacaine and morphine in bitches undergoing ovariohysterectomy.

Study design A parallel, randomized, clinical, prospective and nonblinded study.

Animals A group of 38 Greyhound bitches.

Methods In the catheter group (CathG), CWI with ropivacaine 1% (1 mg kg^{-1} + 0.8 mg kg^{-1} $hour^{-1}$) was applied to the preperitoneal space over the surgical incision. In the epidural group (EpiG), ropivacaine 0.5% (1.3 mg kg^{-1}) and morphine (0.1 mg kg^{-1}) were epidurally administered. Occipital-coccygeal length was used to calculate the volume for the epidural. Pain was scored using a dynamic interactive visual analogue scale (DIVAS) and Glasgow composite measure pain scale–short form (CMPS-SF) before anaesthesia and at 2, 4, 6, 18, 21 and 24 hours after extubation. Incisional sensitivity using a dynamometer (MWTs-incision) was evaluated simultaneously. Plasma ropivacaine and cortisol concentrations, degree of sedation, motor blockade and response to interdigital clamping were measured or assessed. A two-way mixed analysis of variance and a Mann–Whitney *U* test were used to analyse data; $p < 0.05$.

Results No differences were detected in the DIVAS ($p = 0.301$), CMPS-SF ($p = 0.600$) scores, MWTs-incision measurements ($p = 0.257$) and cortisol values ($p = 0.878$) between the groups. Rescue analgesia was required in two dogs, one in each group, at 2 hours. Sedation, motor blockade and negative response to interdigital clamping were detected in EpiG at 2, 4 and 6 hours. Mean plasma ropivacaine values were higher in CathG (0.475 ± 0.164 ng mL^{-1}) than in EpiG (0.184 ± 0.213 ng mL^{-1}; $p = 0.001$).

Conclusion and clinical relevance Compared with epidural ropivacaine and morphine, CWI with preperitoneal ropivacaine is an effective analgesic technique for postoperative pain management in bitches undergoing ovariohysterectomy without motor blockade.

Keywords continuous wound infusion, dogs, epidural, pain management, ropivacaine.

Introduction

Epidural anaesthesia allows postoperative pain management with the use of different drugs, such as opioids, local anaesthetics or α_2-adrenoceptor agonists (DeRossi et al. 2016; Steagall et al. 2017; Garcia-Pereira 2018). Although it is a commonly used technique, complications such as hypotension, bradycardia, ventilatory depression or urinary retention have been reported (Jones 2001; Cerasoli et al. 2017). Moreover, epidural anaesthesia produces temporary motor block (Adami et al. 2012).

A single dose of a local anaesthetic administered via intraperitoneal injection has been used to manage postoperative pain in dogs (Kim et al. 2012; Kalchofner Guerrero et al. 2016). However, studies in humans (Kahokehr et al. 2011;

Fustran et al. 2015) have indicated that a continuous wound infusion (CWI) provides effective postoperative analgesia and reduces hospitalization times and opioid requirements (Liang et al. 2019; Paladini et al. 2020). In veterinary science, CWIs with lidocaine in the preperitoneal space is effective for postoperative pain management in bitches following ovariohysterectomy (Morgaz et al. 2014). Studies in humans have demonstrated that the analgesic effect of CWI and epidural anaesthesia are similar when used following abdominal surgeries (Fassoulaki et al. 2014; Thangavel et al. 2019). To the authors' knowledge, this type of study has not been performed in veterinary medicine.

Therefore, in this study we assessed the postoperative analgesic efficacy of a CWI of ropivacaine administered into the preperitoneal space over the surgical incision in bitches undergoing ovariohysterectomy. This use of CWI ropivacaine was compared with the epidural administration of ropivacaine and morphine. We hypothesized that the two techniques would provide adequate and comparable postoperative analgesia.

Materials and methods

Animals and sample size

This research was approved by the bioethics committee of University of Córdoba (access number: NRS7/2019) and owners provided written informed consent before their dogs participated in this study. The study was conducted in compliance with the CONSORT guidelines for randomized controlled trials.

This research was a parallel, randomized, clinical, prospective and nonblinded study. Healthy adult female Greyhound dogs undergoing elective ovariohysterectomy were included in the study. All dogs had normal haematological, biochemical and electrocardiographic findings prior to inclusion in the study. Pregnant or lactating bitches or dogs with coagulopathies, arrhythmias, systemic diseases or those given analgesic medication within 10 days prior to surgery were excluded.

A prospective power analysis was performed to determine the number of dogs required to document a change of 3 points in the short form of the Glasgow composite measure pain scale (CMPS-SF), with a standard deviation (SD) of 3.3 (Morgaz et al. 2014). The results of this analysis confirmed that with a level of significance of 0.05 and a statistical power of 0.8, a minimum of 16 dogs would be required in each group. Considering potential losses of 15% during the study, 19 dogs were finally included in each group.

Anaesthetic protocol

Animals were fasted for 12 hours preoperatively. The dogs were premedicated with dexmedetomidine (4 μg kg^{-1}, Dexdomitor; Ecuphar, Spain) and morphine (0.3 mg kg^{-1}, Morfina; B. Braun, Spain) mixed in the same syringe and administered intramuscularly. Next, a 20 gauge catheter (20G, Vasovet; B. Braun, Germany) was placed in a cephalic vein for drug and fluid administration (Ringer's lactate solution, 5 mL kg^{-1} $hour^{-1}$) during surgery. At 20 minutes after premedication, animals were preoxygenated via a face mask (A.M.Bickford, NY, USA) for 5 minutes. Anaesthesia was induced with propofol (Propofol Lipuro; B. Braun, Spain) administered intravenously (IV) until there was loss of palpebral and swallowing reflexes, and then the trachea was intubated, and animals were connected to an adult-size rebreathing circle system (McLinely type 3; Everest Veterinary Technology, Spain). Dogs were positioned in dorsal recumbency, and anaesthesia was maintained with isoflurane (IsoVet; B. Braun, Spain) vaporized in an air (40%) and oxygen (60%) admixture. An experienced anaesthesiologist adjusted the dose of isoflurane according to clinical conditions (dilation of pupils, loss of nociceptive autonomic reflexes, loss of palpebral reflex, presence of corneal reflex and eye position) to maintain an appropriate anaesthetic plane during the procedure. Mechanical ventilation was initiated if end-tidal carbon dioxide ($P_E'CO_2$) was > 45 mmHg (6 kPa). Body temperature was maintained between 37 °C and 38.5 °C using a forced-air heating system (EquatorTM; Smiths Medical ASD, ON, Canada).

During the maintenance of anaesthesia, the following variables were monitored using a multiparametric monitor (VetCare; B. Braun, Germany): heart rate (HR, beats $minute^{-1}$), respiratory rate (f_R, breaths $minute^{-1}$), $P_E'CO_2$ (mmHg), body temperature (°C), haemoglobin oxygen saturation (%) and noninvasive systemic arterial pressures (SAP, mmHg). If there was a sudden change in the HR, f_R or SAP and the anaesthetist observed signs of a nociceptive response to surgery, a dose of 2 μg kg^{-1} fentanyl (Fentanest; Kern Pharma, Spain) was administered IV. The number of times intraoperative rescue analgesia was administered was recorded in each group. All animals were administered IV a dose of 0.5 μg kg^{-1} dexmedetomidine at the end of surgery to avoid a dysphoric recovery from anaesthesia. Anaesthetic and surgical times were recorded.

Study groups

The animals were divided into two groups using a random number generator (https://www.randomizer.org. Access date: 10 December 2019), which created a random sequence of 38 numbers assigned in two sets (EpiG and CathG) of 19 unique numbers. Each number in the sequence corresponded to the individual's entry number to the study. Each number from 1 to 38 was assigned to one of the two groups, and after the assignment, a list was created with the group each dog was assigned to. Ovariohysterectomy was performed by two experienced surgeons using a ventral midline incision. In the catheter group (CathG), once the parietal peritoneum was closed, a

wound infusion catheter (5 F nasogastric tube; Securmed, Italy) was introduced between the parietal peritoneum and the abdominal musculature (preperitoneal space) through a small skin incision cranial to the surgical incision. The wound infusion catheter was manually fenestrated on both sides with a 21 gauge needle (Sterican; B. Braun, Spain) at 10 mm intervals aseptically by the surgeon to occupy the entire length of the incision. A monofilament absorbable suture (Monoplus; B. Braun, Spain) closed the rectus abdominis muscle and sheath with a simple continuous pattern, thus covering the wound catheter. Later, a loading dose of ropivacaine (Ropivacaina 1%; B. Braun, Spain) at 1 mg kg^{-1} was administered, followed by a continuous rate infusion of 0.8 mg kg^{-1} $hour^{-1}$ using an elastomeric pump (Administration Pump; Mila International INC, KY, USA). The fixed dose of ropivacaine in the elastomeric pump was mixed with saline and administered at an infusion rate of 2.5 mL $hour^{-1}$ for 24 hours.

In the epidural group (EpiG), after the induction of anaesthesia, the animal was positioned in sternal recumbency. The pelvic limbs were extended cranially to identify the lumbosacral space. The lumbosacral area was clipped and surgically prepared. The same anaesthetist always performed the epidural punctures. A nerve stimulator (Stimuplex HNS 11; B.Braun, Germany) was used to identify the epidural space (Garcia-Pereira 2018). The needle was introduced between the spinal apophysis of the seventh lumbar (L7) and first sacral vertebrae (S1) using an electric current of 0.7 mA. The epidural space was confirmed by observing gross twitches of the pelvic limbs and tail with a loss of resistance test. The response was positive with an electric current of 0.4 mA and negative with 0.2 mA. After the epidural space was correctly identified, the needle hub was checked for the presence of cerebrospinal fluid or blood, and ropivacaine 1% (1.3 mg kg^{-1}) and morphine (0.1 mg kg^{-1}) diluted with saline (50% dilution) were injected slowly. Following dilution, the final concentration of ropivacaine was 0.5%. The animals were maintained in sternal recumbency for 15 minutes. Total vertebral column length (LOC) (distance from the occipital condyle to the first coccygeal vertebra) was measured in each animal. Using this value, the final volume of ropivacaine and morphine for the epidural was calculated according to Valverde and Skelding (2019). This epidural volume was considered suitable to reach the origin of the innervation of the ovaries. Since the volume obtained from the ropivacaine—morphine mixture was always less than this value, it was necessary to add saline (FisioVet NaCl 0.9; B. Braun, Spain) (50% of final volume) to reach the final volume for administration.

Pain evaluation and rescue analgesia

Pain assessment and the measurement of HR, f_R and rectal temperature (RT) were performed at baseline (before premedication) and 2, 4, 6, 18, 21 and 24 hours after extubation. Tracheal extubation (time 0) was performed after the animals regained the ability to swallow and protect their airways. Several pain assessment systems were used: a dynamic and interactive visual analogue scale (DIVAS), the CMPS-SF and measurement of the mechanical wound thresholds (MWTs) using a force dynamometer (PCE-FM50; PCE Instruments, Spain). The mechanical stimulus was applied perpendicular to the skin with a 1 cm^2 round tip. For this measurement, the researcher slowly and progressively increased the manually applied force at the tip. The same researcher, with experience in the use of the dynamometer and trained by the manufacturer, was responsible for all of the MWT measurements. A total of three measurements (cranial, intermediate, caudal) were obtained in close proximity to the surgical incision (MWTs-incision). As a negative control and to ensure correct operation of the device and to detect an excessive response to stimulus, three measurements were performed on the fourth metacarpal bone of the thoracic limb (MWTs-limb). In both cases, a mean value of the three measurements was obtained. Any sudden movement of the animal such as shaking the head, withdrawing the limb, vocalization or attempting to bite were considered a positive response and the end point of measurement. To avoid animal injury, the researcher stopped the measurement when the force applied was 20 N. Values greater than 15 N were considered to be a complete absence of pain.

If the CMPS-SF score was $\geq$ 5/20 (animals unable to walk) or $\geq$ 6/24 (animals able to walk), 0.2 mg kg^{-1} methadone IV (Metasedin; Esteve Pharmaceuticals, Spain) was administered as a rescue analgesic and the animal was excluded from the study. Pain evaluation was performed by the same experienced anaesthetist and in the same sequence: DIVAS, CMPS-SF, MWTs-incision, MWTs-limb, measurement of HR, f_R and RT, and blood sampling (at the times it was taken). The presence of the wound catheter prevented the blinded pain assessment.

Sedation assessment, motor block and clamping response

The level of sedation, motor block and response to clamping were evaluated at 2, 4, 6, 18, 21 and 24 hours after extubation. For assessment of sedation, a semiquantitative scale (Bell et al. 2011) was used with 0 as no sedation and 3 as profound sedation. The degree of motor block was evaluated in three categories: 1, normal (able to stand normally on limbs); 2, moderate motor block (weakness in limbs); 3, complete motor block (complete paralysis of limbs). The response to interdigital clamping was evaluated using forceps at each time point. For this, a Halsted forceps (Aesculap, Germany) was closed (two notches) in the interdigital space between the second and third digit of the pelvic limbs. The clamping was always performed by the same researcher.

Adverse events such as vomiting, tremors, ataxia, bradycardia (HR < 40 beats minute^{-1}), seizures, urinary retention and any other complications were recorded.

Cortisol and ropivacaine determination

A total of 2 mL of venous blood sample was taken by intermittent venepuncture of the jugular vein. This blood was used for the measurement of cortisol and ropivacaine plasma concentrations. Cortisol levels were determined using a chemiluminescent competitive solid-phase enzyme immunoassay (Inmmulite; Siemens Medical Solutions Diagnostics, Germany) at baseline and 2, 6, 18 and 24 hours after extubation. Plasma concentrations of ropivacaine were measured at 1, 2, 6, 18 and 24 hours from extubation using a modified high-performance liquid chromatography method (Gaudreault et al. 2009). Lower limits of quantification and detection for ropivacaine were 25 and 10 ng mL^{-1}, respectively.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows Version 25.0 (IBM Corp, NY, USA). Data normality was evaluated using Shapiro–Wilk test. Normally distributed variables were evaluated by a two-way mixed analysis of variance using the group as the between-subjects factor and time as the within-subjects factor, with a Bonferroni test as *post hoc* analysis. Non-normally distributed data were analysed between groups at each time point using Mann–Whitney *U* test. A Friedman test was used to detect differences in these variables within the same group, and if significant differences were detected, a Wilcoxon test was performed. When an animal required rescue analgesia, it was excluded from further analysis. An independent sample *t* test was used to detect differences between groups in anaesthetic and surgical times, and incisional length. A Chi-square test was used to compare the number of animals receiving intraoperative fentanyl, rescue analgesia, sedation scores, motor block or rates of complications between groups. Normally distributed variables are reported as mean ± SD, non-normally distributed variables as median (25th to 75th percentile) and categorical variables as percentages. Statistical significance was set at $p < 0.05$.

Results

A total of 39 dogs (21 ± 3 kg of mean weight and 3 ± 1 years old of age) were initially enrolled in the study. A dog in CathG was excluded because the animal removed the catheter itself in the early postoperative period. This event occurred 20 minutes after extubation and therefore no postoperative assessments could be performed. For this reason, the next dog enrolled in the study took the place of the excluded animal on the list of randomized group assignments.

In EpiG, the mean value of LOC was 83.8 ± 1.9 cm and the mean epidural volume was 9.2 ± 0.2 mL. No significant differences were observed between groups at any time with regard to HR ($p = 0.063$), f_R ($p = 0.792$) or RT ($p = 0.695$) (Table 1). During anaesthesia, three animals in EpiG and seven in CathG needed fentanyl, no significant differences were detected between groups ($p = 0.141$). In the EpiG, six animals showed signs of mild sedation at 2 hours after extubation ($n =$ 6/19; 31.6%), one of which remained sedated until 6 hours. No animals in CathG showed signs of sedation in the postoperative period. No differences were observed in the length of incision between groups (EpiG: 9.3 ± 1.8 cm; CathG: 9.2 ± 0.8 cm; $p = 0.813$). No other adverse effects related to the drugs used were detected in any group. No differences were detected between groups in the duration of anaesthesia (EpiG: 89.2 ± 24.8 minutes; CathG: 79.1 ± 39.6 minutes; $p = 0.551$) and surgical time (EpiG: 33.9 ± 9.6 minutes; CathG: 28.8 ± 6.5 minutes; $p = 0.364$).

There were no significant differences in the requirement for rescue analgesia between groups because only two animals, one from each group, required methadone 2 hours after extubation. No differences were detected at any time in DIVAS ($p = 0.301$), CMPS-SF ($p = 0.600$) score or in the MWTs-limb measurements ($p = 0.193$), with all values associated with adequate analgesia. No differences in MWTs-incision measurements ($p = 0.257$) were observed between groups at any time, although in both groups a significant reduction in these values were detected at 2, 6 and 18 hours compared with baseline. Nevertheless, the mean values of MWTs-incision remained at approximately 15 N during the postoperative period and animals were comfortable when measurements were performed.

No differences in the plasma cortisol levels were detected between groups at the same time points ($p = 0.878$). A significant increase in cortisol was detected at 2 hours when compared with baseline in EpiG [3.74 μg dL^{-1}: 95% confidence interval (CI), 0.87–6.60 μg dL^{-1}; $p = 0.006$] and CathG (3.30 μg dL^{-1}: 95% CI, 0.28–6.31 μg dL^{-1}; $p = 0.026$). At later times, plasma cortisol values decreased progressively and at 24 hours, these values were not significantly different from those measured at baseline ($p = 0.999$).

At 2 hours, nine animals in EpiG showed partial motor block ($n = 9/19$; 47.3%) and five total motor block ($n = 5/19$; 26.3%). At 4 hours, four animals had partial motor block ($n =$ 4/19; 21.1%) and two had total motor block ($n = 2/19$; 10.5%), whereas at 6 hours only three had partial motor block ($n = 3/19$; 17.8%) and one had complete motor block ($n = 1/$ 19; 5.2%). From 18 hours postextubation, animals in EpiG no longer showed any signs of motor block, whereas no animals in CathG had motor deficits during the entire postoperative period. Hence, there were significant differences in the presence of motor blockade at 2, 4 and 6 hours. Negative responses

Table 1 Values of heart rate (HR), respiratory rate (f_R), rectal temperature (RT), the short form of the Glasgow composition measure pain scale (CMPS-SF) scores, dynamic and interactive visual analogue scale (DIVAS) scores, mechanical wound thresholds measurements (MWTs-limb and MWTs-incision) and cortisol concentrations. Measurements were made at baseline, and 2, 4, 6, 18, 21 and 24 hours after extubation in two groups of dogs (18 animals in each group). Animals in the catheter group (Catheter) were given ropivacaine (0.8 mg kg^{-1} hour^{-1}) and dogs in the epidural group (Epidural) were given ropivacaine (1.3 mg kg^{-1}) and morphine (0.1 mg kg^{-1}). Normally distributed variables are expressed as means ± standard deviation (SD) and non-parametric data as median (25th to 75th percentile)

Variable	Group	Before anaesthesia	2 hours	4 hours	6 hours	18 hours	21 hours	24 hours
HR (beats minute^{-1})	Epidural	87 ± 12	76 ± 19	71 ± 15	79 ± 18	87 ± 26	89 ± 26	84 ± 21
	Catheter	97 ± 20	79 ± 17	80 ± 17	81 ± 18	87 ± 25	76 ± 15	80 ± 15
f_R (breaths minute^{-1})	Epidural	22 ± 5	22 ± 8	20 ± 6	20 ± 5	24 ± 7	20 ± 8	20 ± 6
	Catheter	24 ± 6	24 ± 8	22 ± 6	22 ± 7	22 ± 8	22 ± 7	26 ± 11
RT (°C)	Epidural	38.2 ± 0.4	37.1 ± 0.6	37.6 ± 0.7	38.1 ± 0.5	37.9 ± 0.4	37.9 ± 0.5	37.8 ± 0.5
	Catheter	38.2 ± 0.4	37.3 ± 0.7	38.0 ± 0.4	38.2 ± 0.4	38.1 ± 0.4	38.0 ± 0.4	38.0 ± 0.3
CMPS-SF	Epidural	0 (0)	2 (1–3)	2 (1–2)	2 (1–3)	1 (1–2)	1 (0–2.25)	1 (0–1)
	Catheter	0 (0)	2.5 (0–4)	1 (0–3)	2 (0–3)	1 (0–2)	1 (0–2)	0 (0–2)
DIVAS (cm)	Epidural	0 ± 0	1.8 ± 1.7	1.8 ± 1.8	1.8 ± 2.0	1.0 ± 1.3	1.0 ± 1.8	0.5 ± 0.9
	Catheter	0 ± 0	2.5 ± 2.7	1.5 ± 1.7	1.3 ± 1.6	1.1 ± 1.6	1.1 ± 1.5	0.8 ± 1.3
MWTs-limb (N)	Epidural	21.7 ± 7.7	19.9 ± 7.9	20.5 ± 7.7	18.3 ± 9.5	20.0 ± 9.6	18.5 ± 7.5	19.7 ± 8.8
	Catheter	23.7 ± 9.9	21.8 ± 8.4	19.1 ± 7.6	21.4 ± 8.9	19.2 ± 10.2	21.5 ± 9.5	21.2 ± 8.2
MWTs-incision (N)	Epidural	19.5 ± 4.7*'†'‡	16.2 ± 4.7	15.8 ± 5.2*	14.5 ± 6.4†	14.8 ± 4.2‡	16.8 ± 4.7	16.4 ± 5.5
	Catheter	20.8 ± 5.6*'†'‡δ	15.5 ± 3.3*	14.6 ± 4.6†	15.5 ± 4.4‡	16.4 ± 3.8δ	17.1 ± 3.8	17.4 ± 3.4
Cortisol (μg dL^{-1})	Epidural	2.34 ± 0.88*'†	6.08 ± 2.83*'‡	—	4.35 ± 1.32†	3.64 ± 1.33	—	2.70 1.09‡
	Catheter	2.48 ± 0.58*'†	5.80 ± 3.41*'‡	—	4.64 ± 1.22†	3.53 ± 1.23	—	2.49 0.81‡

Superscript symbols indicate significant differences between different times in the same group. No differences were detected between groups.

to interdigital clamping were observed in some dogs at 2 hours (n = 15/19; 78.9%), 4 hours (n = 4/19; 21.1%) and 6 hours (n = 1/19; 5.2%) in EpiG. Thereafter, all animals showed positive responses. In CathG, negative responses were not detected after interdigital clamping at any time point.

The mean values of plasma ropivacaine concentrations after epidural administration and intraperitoneal infusion are shown in Fig. 1. The mean values during the postoperative period of plasma ropivacaine were 0.475 ± 0.164 and 0.184 ± 0.213 ng mL^{-1} in CathG and EpiG, respectively. Significant differences were detected in ropivacaine plasma values between groups (p = 0.001), because in EpiG a progressive significant reduction in plasma values were detected from 1 hour until minimum values were reached at 24 hours, whereas in CathG, the constant-rate preperitoneal infusion meant that these values were stable throughout the postoperative period (p = 0.188).

Discussion

The present study showed that the CWI of ropivacaine through a preperitoneal wound catheter provided effective postoperative analgesia in dogs undergoing ovariohysterectomy. A similar effect was produced via the epidural route using ropivacaine and morphine.

Epidural anaesthesia provides anaesthesia and analgesia for procedures of the pelvis, pelvic limbs, perineum and for some abdominal procedures. Its use is associated with minimal cardiopulmonary changes (Garcia-Pereira 2018). In the present study, epidural application of ropivacaine and morphine provided effective analgesia, with low CMPS-SF and DIVAS values. Similar results were observed with MWTs-incision values which were > 15 N, although there was a significant reduction following surgery compared with baseline. Some

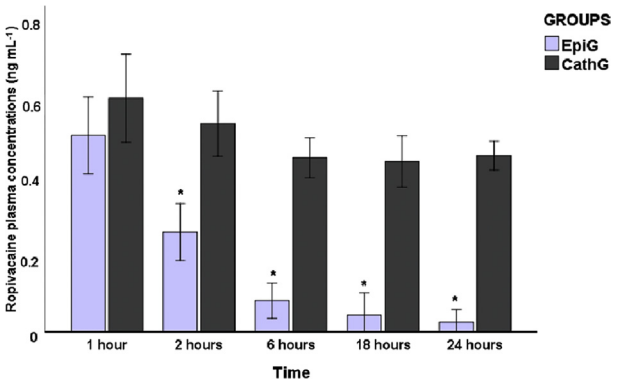

Figure 1 Plasma concentrations of ropivacaine in the catheter (ropivacaine 0.8 mg kg^{-1} hour^{-1}; CathG) and epidural (ropivacaine 1.3 mg kg^{-1} and morphine 0.1 mg kg^{-1}; EpiG) groups during postoperative period. Venous blood samples were taken from 36 dogs (18 animals in each group) to measure plasma concentrations using a modified high-performance liquid chromatography. Bars show the mean values and error bars indicate 95% confidence intervals of the mean values. *Significantly different between groups at a specific time (p < 0.05).

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animals presented values > 20 N. Although the researcher stopped the application of force when it reached the cut-off value of 20 N, this assessment was manual, and this would explain why values were greater than this number. No animals were harmed during the procedure, so we consider that this would have no clinical consequences.

Epidural anaesthesia with only a local anaesthetic produces a short analgesic duration. Therefore, it is frequently combined with opioids to increase the duration and intensity of its analgesic effect (Otero & Campoy 2013; Steagall et al. 2017). For this reason and to ensure an equal duration of effect in both groups, we combined ropivacaine with morphine. The plasma ropivacaine concentrations were significantly less 6 hours after extubation, but the analgesic effect detected in EpiG remained for 24 hours which probably resulted from the inclusion of morphine.

In human medicine, the use of ropivacaine via CWI reduces the need for opioids following different types of surgery (Chaykovska et al. 2014; Raines et al. 2014; Fustran et al. 2015). However, some studies in humans have not found any advantage to the use CWI of ropivacaine after abdominal surgeries (Reinikainen et al. 2014). These differences could result from the site of the wound catheter placement since preperitoneal locations have shown a more intense analgesic effect than subcutaneous wound catheters (Mungroop et al. 2019). In dogs, a single administration of a local anaesthetic via an intraperitoneal injection is commonly used to control postoperative pain (Kim et al. 2012; Kalchofner Guerrero et al. 2016). Nevertheless, postoperative infiltration with bupivacaine over the incision site is not effective for pain control in dogs following ovariohysterectomy (Fitzpatrick et al. 2010). A CWI of lidocaine has shown good results for pain management in female dogs undergoing ovariohysterectomy with low complication rates (Morgaz et al. 2014). To our knowledge, the present study is the first in which a constant-rate preperitoneal infusion of ropivacaine has been used in dogs. Therefore, the infusion dose rate we used was based on previous studies in humans (Eljezi et al. 2017; Oxlund et al. 2018).

Cortisol measurements were included as a stress marker of surgical pain and to complement the other methods of pain assessment we used. No differences were detected in cortisol concentrations between groups. In both groups, the maximum cortisol level was measured at 2 hours; however, according to CMPS-SF, DIVAS and MWTs-incision values, the animals had minimal pain. The increase in cortisol could result from adrenal glucocorticoid stimulation owing to the surgical stress. The cortisol values measured in the present study are similar to those obtained by others researches where spinal anaesthesia and peripheral nerve blocks were effective in reducing the stress responses to surgery (Kim et al. 2012; Romano et al. 2016).

In humans undergoing abdominal surgery, the analgesic effects of CWI and epidural anaesthesia using ropivacaine have been compared and those authors concluded that both techniques were comparable to one another (Fassoulaki et al. 2014; Thangavel et al. 2019). These findings agree with the results of the present study, which is the first one in which CWI and epidural anaesthesia have been compared in dogs. No differences in pain scores were observed in EpiG and CathG, and pain management was considered to be satisfactory in both groups. The provision of effective analgesia when local anaesthetics are used alone is an important benefit of CWI. Current trends in human anaesthesia include the use of opioid-free analgesia techniques, which avoids the potentially harmful effects of opioids such as hyperalgesia or allodynia (Fiore et al. 2019). The administration of ropivacaine as a CWI would offer a promising pain management tool particularly in situations in which opioid-free analgesia could be advisable (White et al. 2017).

In the present study, ropivacaine plasma concentrations decreased rapidly after epidural administration and were within the range reported by other authors, who used the same route of administration and a dose of 1 mg kg^{-1} (Arthur et al. 1988). Conversely, the mean peak ropivacaine plasma concentration was obtained at 1 hour postinjection in CathG, and then a steady state was observed for the remainder of the 24 hours period. This finding suggests that continuous peritoneal administration provides a constant plasma level, as previously described in humans with ropivacaine (Beaussier et al. 2007). Plasma concentration values $\geq$ 11.4 μg mL^{-1} produce convulsions after the IV administration of ropivacaine (Feldman et al. 1989). None of the concentrations measured in this assay reached those values, with maximum concentrations of 0.55 and 0.80 ng mL^{-1} after epidural administration and intraperitoneal infusion, respectively. These results and the absence of local or systemic adverse reactions after CWI suggest that intraperitoneal infusion of ropivacaine is safe and effective.

Complications of epidural administration include spinal injection, pruritus or urine retention (Otero & Campoy 2013; Cerasoli et al. 2017). Although none of these complications occurred in the present study, a slower recovery was observed in EpiG with 31.6% of dogs still showing signs of sedation at 2 hours, while some dogs had motor blockade and no responses to interdigital clamping for up to 6 hours. Since the same premedication drugs were used in the two groups and none of the animals in CathG were sedated postoperatively, we propose that epidural drug administration caused sedation. This could be due to a pharmacologic effect of circulating drugs absorbed from the epidural space or by a reduction in sensory input to the nervous system (Hannallah & Mundt 1994). The only inconvenience encountered in the CathG was early removal of

the catheter by one animal, which has been observed in a previous study (Morgaz et al. 2014).

The main limitation of the present study was that it was not blinded. The presence of the wound catheter meant that the assessor knew the allocated group for each animal. We tried to minimize this limitation by using different scales and methods of pain measurement. Another limitation is the fact that we did not use a Tuohy needle for epidural drug administration, instead the epidural space was identified using a nerve stimulator and drugs were administered via that needle. Although we used the nerve stimulation technique, we cannot exclude the possibility that the need for rescue analgesia in EpiG resulted from incorrect positioning of the needle tip during epidural injection.

Conclusions

The continuous administration of ropivacaine in the preperitoneal space via wound soaker catheters is an effective and safe method of postoperative pain management in female Greyhounds dogs undergoing ovariohysterectomy, providing similar analgesic effects to epidural with ropivacaine and morphine, but without the resulting motor block.

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Authors' contributions

JM and RNC: study conception and design, data acquisition, analysis and interpretation of results, statistical and ropivacaine analysis, manuscript preparation, critical revision. DFT: data acquisition, analysis and interpretation of results, manuscript preparation, critical revision. MMG, SQC and JAFS: data acquisition, analysis and interpretation of results. JMSR: statistical and ropivacaine analysis. JMD: manuscript preparation and critical revision. All authors approved the final article.

Conflict of interest statement

The authors declare no conflict of interest.

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