Intraperitoneal and incisional ropivacaine did not improve postoperative analgesia after multimodal anaesthesia compared with saline in dogs undergoing ovariohysterectomy

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Die Postoperative Analgesie einer Ovariohysterektomie mit multimodaler Anästhesie bei Hunden wurde durch intraperitoneal und inzisional verabreichtes Ropivacain im Vergleich zu Kochsalzlösung nicht verbessert

Die intraperitoneale Verabreichung von Lokalanästhetika kann postoperativen Schmerzen nach einer Ovariohysterektomie bei Hunden lindern. Das Ziel dieser prospektiven, randomisierten, verblindeten, Placebo kontrollierten klinischen Studie war der Vergleich der postoperativen Analgesie und des Opioidbedarfs nach intraperitonealer und inzisionaler Verabreichung von Ropivacain im Vergleich zu 0,9 % NaCl (Kochsalzlösung).

In die Studie wurden 43 Hunde aufgenommen und nach einem standardisierten Protokoll mittels intramuskuläre Prämedikation (0,03–0,05 mg/kg Acepromazin, 0,01 mg/kg Dexmedetomidin 0,01 mg/kg) und mit auf die Wirkung eingestelltem Propofol und Ketamin (1 mg/kg) intravenös eingeleitet, sowie die Anästhesie mit Isofluran in Sauerstoff aufrechterhalten. Das analgetische Regime umfasste Carprofen (4 mg/kg) subkutan und Morphin (0,2 mg/kg) intravenös. Abhängig von der Gruppenzuordnung erhielt jeder Hund entweder eine intraperitoneale und inzisionele Verabreichung von Ropivacain (2 mg/kg bzw. 1 mg/kg) (Gruppe R) oder eine gleiche Menge Kochsalzlösung (Gruppe S). Bei Entfernung der Gebärmutter wurde zusätzlich Buprenorphin (0,02 mg/kg) intramuskulär verabreicht. Sedierung und Schmerzen wurden 0,5, 1, 2, 4, 6 und 8 Stunden nach der Extubation anhand einer Sedierungsskala, der Kurzform der Glasgow Composite Pain Scale (CMPS-SF) und einer dynamischen interaktiven visuellen Analogskala (DIVAS) bewertet. Postoperativ

Summary

Intraperitoneal administration of local anaesthetics may reduce postoperative pain after ovariohysterectomy in dogs. The aim of this prospective, randomised, blinded, placebo-controlled clinical trial was to compare postoperative analgesia and opioid requirements after intraperitoneal and incisional administration of ropivacaine versus 0,9 % NaCl (saline).

Forty-three client-owned dogs were enrolled in the study and anaesthetised using a standardized protocol that included premedication with acepromazine (0,03–0,05 mg/kg) and dexmedetomidine (0,01 mg/kg) intramuscularly. Anaesthesia was induced with propofol titrated to effect and ketamine (1 mg/kg) intravenously and maintained with isoflurane in oxygen. The analgesic regimen included carprofen (4 mg/kg) subcutaneously and morphine (0,2 mg/kg) intravenously. Depending on group assignment, each dog received either an intraperitoneal and incisional splash with ropivacaine (2 mg/kg and 1 mg/kg, respectively) (group R), or an equal volume of saline (group S). Buprenorphine (0,02 mg/kg) was administered intramuscularly once the uterus was removed. Sedation and pain were assessed 0,5, 1, 2, 4, 6 and 8 hours after extubation using a sedation scale, the short form of the Glasgow Composite Pain Scale (CMPS-SF) and a dynamic interactive visual analogue scale (DIVAS). Postoperatively, buprenorphine (0,01 mg/kg) was administered intravenously if dogs scored 6/24 on CMPS-SF.

The ordinal mixed model showed no difference in pain scores between groups. Fisher's exact test showed no significant difference in postoperative buprenorphine requirements between group S (3/22 dogs) and group R (1/21 dogs) at the doses used. In addition, lower sedation scores were associated with higher DIVAS scores.

wurde Buprenorphin (0,01 mg/kg) intravenös verabreicht, wenn die Hunde im CMPS-SF einen Wert von 6/24 erreichten.

Das ordinale gemischte Modell zeigte keinen Unterschied in den Schmerzwerten zwischen den Gruppen. Der Exakte Fisher-Test zeigte bei den verwendeten Dosen keinen signifikanten Unterschied im postoperativen Buprenorphinbedarf zwischen Gruppe S (3/22 Hunde) und Gruppe R (1/21 Hunde). Darüber hinaus waren niedrigere Sedierungswerte mit höheren DIVAS-Werten verbunden.

In diesem multimodalen Analgetikaprotokoll konnte Ropivacain die Analgesie im Vergleich zu Kochsalzlösung nicht verbessern.

Schlüsselwörter: Anästhesie, Hund, Kastration, lokal, Ovariohysterektomie, Spritzblock

In this multimodal analgesic protocol, ropivacaine could not improve analgesia compared to saline.

Keywords: anaesthesia, canine, castration, locoregional, spay, splash block

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Introduction

Ovariohysterectomy (OVH) is one of the most commonly performed surgical procedures in dogs and cats and can result in mild to moderate pain in the postoperative period.[3,14] Postoperative pain can have several negative effects including delay in recovery, increased length of hospitalization, decreased appetite, increased protein catabolism, impaired respiratory function, increased risk of infection and the development of chronic pain.[30,31]

For patients suffering from pain, adequate analgesia is critical to provide optimal care.[27] Traditionally, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids have been the drugs of choice to treat postoperative pain in veterinary patients, but their use is associated with non-negligible negative side effects.[13,37] To reduce these side effects, recent recommendations for pain management include the use of local anaesthetics in the majority of surgical procedures.[11] Their potential to significantly attenuate both intraoperative and postoperative pain may therefore reduce a patient's opioid consumption.[29] In addition, the Global Pain Council of the World Small Animal Veterinary Association advocates the intraperitoneal (IP) use of local anaesthetics for postoperative pain management after visceral surgery in dogs and cats as part of a multimodal analgesic approach.[34]

Previous studies have shown that direct IP administration of lidocaine or bupivacaine in dogs following OVH results in a reduction in postoperative pain following OVH in dogs[3,20] while others found no significant or clinically relevant differences.[2,22]

Ropivacaine is a long-acting amide-type local anaesthetic that is structurally similar to bupivacaine but is synthesized as an S-enantiomer.[23] In a rat model, the toxic potential for the central nervous system and heart was lower with ropivacaine than with bupivacaine, therefore, the risk of adverse effects is lower.[5] In one study 3 mg/kg ropivacaine administered IP produced comparable postoperative analgesia to bupivacaine in dogs after OVH.[25] In contrast, when 1 mg/kg ropivacaine IP was compared with saline, no differences in the postoperative period were observed.[20] Although ropivacaine appears to be safer and promising, there is limited evidence to support its IP use. Therefore, the aim of this study was to evaluate postoperative analgesia and opioid requirements in dogs undergoing OVH and receiving either ropivacaine or saline IP and INC. We hypothesized that IP and INC ropivacaine would result in lower postoperative pain scores and opioid requirements compared to saline.

Materials and methods:

Study design

Ethical approval for this prospective, randomized, blinded, placebo-controlled clinical trial was obtained from the Institutional Animal Care and Use Committee of St George's University, Grenada (IACUC-22002-R).

Randomization to a ropivacaine (Group R) or a saline group (Group S) was performed by a single investigator (BS) by drawing lots from an envelope. All other researchers were blinded to the respective treatment.

Animals

Client-owned healthy female dogs admitted to the veterinary teaching hospital for OVH were screened for eligibility to participate in the study. Written informed owner consent was obtained for each dog enrolled. Only dogs that were easy to handle, friendly and considered healthy based

on clinical examination and haemato-biochemical parameters were included. Exclusion criteria were aggressiveness, pregnancy, positive tests for *Ehrlichia canis, Borrelia burgdorferi, Dirofilaria immitis* and/or *Anaplasma phagocytophilum* (Snap 4 Dx, IDEXX Laboratories, Dr Westbrook, ME 04092, USA), pain due to pre-existing medical conditions or preoperative treatment with analgesics that were not part of the anaesthetic protocol. Breed, age, and body weight were recorded.

Anaesthesia and surgery

Food, but not water, was withheld overnight. On the day of surgery, all dogs were premedicated with 0,03–0,05 mg/kg acepromazine (Acepromazine; 100 mg/ml, VetOne, Corporate Headquarters, 3041 West Pasadena Drive Boise, Idaho 8370, USA) and 0,01 mg/kg dexmedetomidine (Dexdomitor; 0,5 mg/ml, Provet AG, Gewerbestrasse 1, 3421 Lyssach, Switzerland) administered intramuscularly (IM). Twenty minutes later, an appropriate size intravenous (IV) catheter (Surflo; Terumo Medical Products, 265 Davidson Avenue Somerset, NJ 08873, USA) was aseptically placed in a cephalic vein and anaesthesia was co-induced with 1 mg/kg propofol (Indifol-200 Propofol injection; 10 mg/ml, Varenyam, Healthcare Pvt Ltd, GF & FF, Tower-H, Sunwelkin, near IOC Petrol Pump, Harni, Vadodara, Gujarat 390022, India) and 1 mg/kg ketamine (Ketamine hydrochloride; 50 mg/ml, Rotexmedica GmbH Arzneimittelwerk, Bunsenstrasse 4, 22946 Trittau, Germany) IV. The level of anesthesia was evaluated, and additional boluses of propofol, each containing 0,5 mg/kg, were given until smooth endotracheal intubation was possible. The total amount of propofol administered was recorded.

Anaesthesia was maintained with isoflurane (Fluriso; VetOne, Corporate Headquarters, 3041 West Pasadena Drive Boise, Idaho 8370, USA) in oxygen administered via an anaesthesia machine (MDS Matrx; VMS Anesthesia Machine, 145 Mid Country Drive, Orchard Park, NY 14127, USA). The dogs remained in spontaneous ventilation. A paediatric circular rebreathing system was used in dogs with body weight <7 kg, and a coaxial rebreathing system in dogs weighing >7 kg.

During aseptic preparation of the surgical field, 4 mg/kg carprofen (Rimadyl Zoetis Inc.; 50 mg/ml, 333 Portage Street, Kalamazoo, MI 49007, USA) was administered subcutaneously (SC).

In the operating theatre, all dogs received 0,2 mg/kg morphine (Morphine Sulfate injection BP; 10 mg/ml, Macarthys Laboratories t/a Martindale Pharma Bampton Road Harold Hill Romford RM3 8UG, UK) IV over five minutes. Lactated Ringer's solution (Lactated Ringer's injection USP; Baxter Healthcare Corporation, One Baxter Parkway Deerfield, IL 60015, USA) was administered throughout anaesthesia IV at a rate of 5 ml/kg/h. Heart rate (HR), respiratory rate (RR), electrocardiography, end-tidal carbon dioxide, peripheral haemoglobin oxygen saturation, non-invasive blood pressure and body temperature were monitored intraoperatively using a multiparametric monitor (BM5Vet; Bionet America Inc.,2691 Dow Ave B, Tustin, CA 92780, USA). In addition, an oesophageal stethoscope was inserted into the dogs' oesophagus and a probe from a Doppler ultrasound flow detector was placed on clipped skin over the radial artery.

Third-year veterinary students performed both anaesthesia and OVH under close supervision of experienced anaesthetists and surgeons. The depth of anaesthesia was adjusted by increasing or decreasing the dose of isoflurane based on clinical assessment and monitored parameters. If required, additional analgesia with fentanyl (Fentanyl injection; 0,05 mg/ml, Macarthys Laboratories t/a Martindale Pharma Bampton Road Harold Hill Romford, RM3 8UG, UK) IV was administered at the discretion of a senior anaesthetist. The total amount of fentanyl used during general anaesthesia was recorded for each dog. Hypotension was treated by reducing the volume percentage of isoflurane delivered and/or by bolus administration of 5 ml/kg Lactated Ringer's solution IV over five minutes.

After the uterus was removed, all dogs received 0,02 mg/kg buprenorphine (Vetergesic; 0,03 mg/ml Ceva Animal Health Inc. 6–1040 Fountain St. N., Cambridge, ON, N3E 1A3, Canada) IM.

Prior to complete closure of the linea alba, 2 mg/kg ropivacaine 0,75 % (Ropivacain Sintetica; Sintetica SA, Via Penate 5, 6850, Mendrisio, Switzerland) (Group R), or an equal volume (0,27 ml/kg) of saline (0,9 % Sodium Chloride injection USP; Baxter Healthcare Corporation, One Baxter Parkway Deerfield, IL 60015, USA) (Group S) was administered IP using an 18-gauge IV catheter after the stylet was removed. The administration of the treatment was performed by the assisting student during the surgery who was blinded to assigned treatments. The tip of the catheter was inserted into the peritoneal cavity at the cranial end of the surgical incision. The drug was administered in a windscreen wiper motion spreading the drug from the cranial to the caudal abdomen. For the INC splash, an additional 1 mg/kg ropivacaine (group R) or an equal volume (0,13 ml/kg) of saline (group S) was dripped onto the incision line after closure of the linea alba.

The isoflurane was discontinued as soon as the skin closure was completed. The duration of surgery and anaesthesia and any complications encountered were noted. The length of the incision (LOI) and the distance from the xiphoid to the os pubis (DXOP) were measured and their ratio calculated as LOI/DXOP. Extubation was performed as soon as the swallowing reflex was apparent, and the time was noted as T0.

Postoperative assessment

Postoperative monitoring was performed by a single observer (KKL) blinded to all IP and INC treatments, at fixed time points after extubation (T0,5 = 30 minutes, T1 = one hour, T2 = two hours, T4 = four hours, T6 = six hours, T8 = eight hours).

For assessment of sedation, a validated 7-item scale was used.[10,46] The sedation scale comprises maximum 21 points, with a higher score indicating greater sedation.

Two different pain scoring methods were used: firstly, a dynamic interactive visual analogue scale (DIVAS) on which the assessor marks any point on a straight 100 mm line. A value at the extreme left end represents the absence of pain and a value at the extreme right end represents the worst pain imaginable.[26] Secondly, the short form of the Glasgow Composite Measure Pain Scale (CMPS-SF), a multidimensional pain scale with a maximum of 24 points or 20 points if the dog's mobility cannot be assessed.[38] In addition, the clinical parameters HR and RR were recorded at each time point. Rescue analgesia (0,01 mg/kg buprenorphine IV) was administered when a score of ≥ 5/20 or ≥ 6/24 was reached on CMPS-SF.

Statistical analysis

The sample size was calculated (https://clincalc.com/stats/samplesize.aspx) using an incidence of 0 % versus 30 % for administration of opioids to an individual over a twelve-hour period. With a power of 80 % and an alpha error of 0,05, 21 dogs per group would be required. Data were tested for normality using the Shapiro-Wilk test. Single measurements were compared using either T-test or Mann-Whitney U test.

DIVAS, CMPS-SF and sedation score were analyzed using a cumulative link mixed model fitted with the Laplace approximation with time point as a covariate, group as fixed effect and random effects: time as a random slope and dog as random intercept. Postoperative opioid requirements were compared with Fisher's exact test. Data after administering rescue analgesia were not included in the statistical analysis.

Results

Of a total of 108 female mixed breed dogs anaesthetized and undergoing OVH, 43 met the criteria and were included in the study. Group allocation resulted in 22 dogs in group S (51 %) and 21 dogs in group R (49 %). No difference was found between groups in age, body weight, duration of anaesthesia and surgery, ratio of length of incision (LOI) to distance from xiphoid to os pubis, time to extubation, and time gap between buprenorphine administration and T0 as shown in Table 1.

Sedation score, CMPS-SF score, DIVAS score, and HR did not differ between groups (Table 2). The pain scores for each time point and the scoring system are shown in Figures 1 and 2.

Table 1: Demographic data, duration of anaesthesia and surgery, ratio of length of incision (LOI) to distance from os pubis to xiphoid, time to extubation and time gap in administration of buprenorphine to T0 for 43 dogs undergoing ovariohysterectomy treated with intraperitoneal and incisional ropivacaine (Group R; 21 dogs) or saline (Group S, 22 dogs).

Variable	Group S median (range)	Group R median (range)	p -value
Age (months)	17 (6–96)	24 (5–1,8)	0,49
Body weight (kg)	11,3 (5,1–24,7)	10,3 (5–18,3)	0,33
Anaesthesia duration (minutes)	2,4 (1,0–2,0)	2,9 (1,0–2,8)	0,62
Surgery duration (minutes)	1,9 (1,4–1,5)	1,9 (90–1,3)	0,56
Ratio LOI/distance os pubis to xiphoid (%)	39 (29–53)	38 (30–53)	0,94
Time to extubation (minutes)	8 (1–26)	11 (0–26)	0,79
Time gap administration buprenorphine to T0 (min)	95 (65–1,0)	98 (56–1,1)	0,99

Table 2: Effect of treatment with ropivacaine (Group R) or saline (Group S) on the dynamic interactive visual analogue scale (DIVAS), the Short Form of the Glasgow Composite Measure Pain Scale (CMPS-SF), sedation score and heart rate (HR) in 43 dogs undergoing ovariohysterectomy.

Variable	Effect of treatment Group R vs Group S			
	Estimated effect	Standard error (SE)	Z value	p -value
DIVAS score	0,33	0,54	0,61	0,53
CMPS-SF score	–0,15	0,41	–0,38	0,7
Sedation score	0,055	0,64	0,08	0,93
HR	–9	4,94	39	0,06

The results of this study showed a low incidence (4/43; 9,3 %) of postoperative opioid requirement with no significant difference between groups (p =0,6). In group S, 3/22 dogs (13,6 %) and in group R, 1/21 dogs (4,7 %) received rescue buprenorphine. In group S, two animals received rescue analgesia at T0,5 and one animal at T1, in contrast to one animal at T6 in group R. The sedation scores in group S were 8/21 and 11/21 in the dogs that received rescue buprenorphine at T0,5, and 13/21 at T1, while the dog in group R obtained a score of 4/21 at T6.

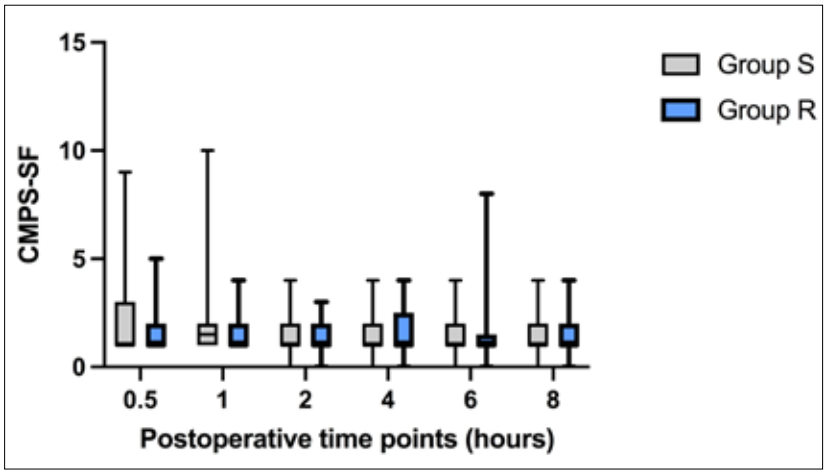

Figure 1: Box-and-whisker plots of the short form of the Glasgow Composite Pain Scale (CMPS – SF) in 43 dogs undergoing ovariohysterectomy. Dogs received 2 mg/kg intraperitoneal and 1 mg/kg incisional ropivacaine (group R) or saline solution in the same volume (group S). Dogs were evaluated from 30 minutes (T0,5) up to eight hours (T8) after extubation. Data collected after administration of rescue analgesia were not included. Each box represents the interquartile range, and the median value is the horizontal line within each box. The lower and upper whiskers represent the minimum and maximum values, respectively.

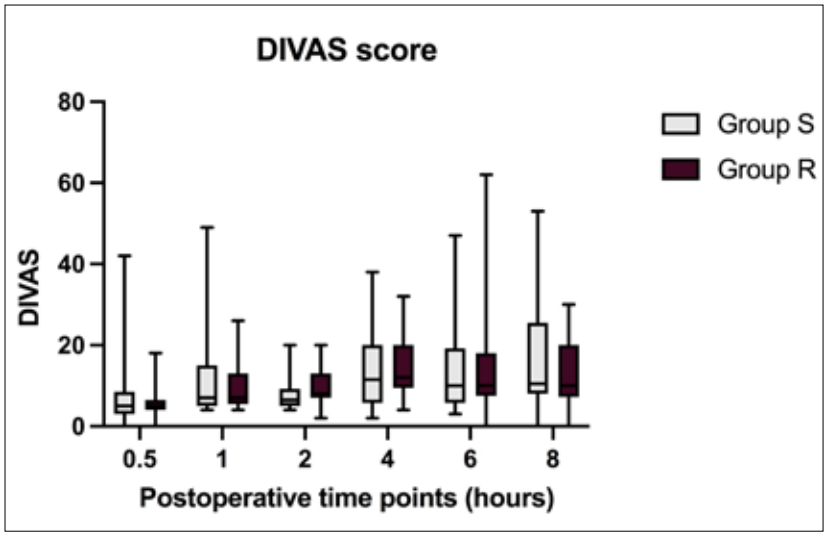

Figure 2: Box-and-whisker plots of the dynamic interactive visual analogue scale (DIVAS) in 43 dogs undergoing ovariohysterectomy. Dogs received 2 mg/kg intraperitoneal and 1 mg/kg incisional ropivacaine (group R) or saline solution in the same volume (group S). Dogs were evaluated from 30 minutes (T0,5) up to eight hours (T8) after extubation. Data collected after administration of rescue analgesia were not included. Each box represents the interquartile range, and the median value is the horizontal line within each box. The lower and upper whiskers represent the minimum and maximum values, respectively.

Sedation score decreased over time (estimate -1,46, (SE 0,148, z -9,88, p < 0,001)) (Figure 3). Although no difference was observed between groups in HR, an increasing trend was detected over time (estimate 2,5, (SE 0,69 z -39, p <0,001)).

There was no association between sedation score and CMPS-SF (estimate -0,09, (SE 0,05, z -0,7, p =0,08)). The CMPS-SF score was positively associated with an increase in RR (estimate 0,02, (SE 0,01, z 2,76, p = 0,005)). A higher sedation score was associated with a lower DIVAS pain score (estimate -0,22, (SE 0,07, z -3,13, p =0,001)). DIVAS increased over time (estimate 0,37, (SE 0,08, z 4,27, p < 0,001)).

Discussion

Contrary to our hypothesis, we were unable to demonstrate any significant benefit of IP and INC ropivacaine compared with saline on postoperative pain scores in dogs undergoing OVH when administered in addition to the systemic analgesic protocol described. The low incidence of rescue opioid requirements (3/22 in group S and 1/21 in group R) makes it difficult to draw conclusions. One possible explanation for the lack of significant difference in opioid use between treatments could be an underpowered study. Our initial sample size calculations were based on an incidence of 0 % versus 30 % for opioid administration to an individual. Repeating the power calculation with the incidence of rescue analgesia in the current study, 160 dogs (80 per group) would have been required to conclusively investigate whether the incidences found were accurate and whether there were no differences in pain scores between groups.

In our study, the three dogs in group S required rescue buprenorphine at T0,5 and T1, while the dog in group R required rescue analgesia at T6. Although the overall requirements for rescue buprenorphine between the groups was not statistically significant, this may indicate a beneficial effect of ropivacaine within the first six postoperative hours. These results are comparable to another study investigating the administration of IP ropivacaine in dogs undergoing OVH where the authors reported an effect over six hours after surgery.[25] These findings may indicate a shorter duration of analgesia with ropivacaine compared to bupivacaine after IP administration. In dogs, a shorter duration of brachial plexus nerve block performed with 2 or 3 mg/kg ropivacaine (275 minutes) compared to 2 mg/kg bupivacaine (387 minutes) has already been reported.[39] Studies on humans, in contrast, demonstrate a longer duration of action for ropivacaine, lasting for 13 hours after laparoscopic cholecystectomy.[4] While species-specific dif-

ferences must be taken into consideration, the different ways of drug administration and different pain scorings methods in different studies might affect the results obtained.

The anaesthetic protocol used in the current study contained several analgesics and anaesthetics with analgesic properties. A synergistic analgesic effect has been demonstrated for the combination of an opioid morphine and dexmedetomidine, resulting in lower postoperative pain scores in dogs undergoing OVH.[19] In our study, buprenorphine was the opioid of choice due to limited availability of other shorter acting opioids. Notably, buprenorphine was administered IM around 90 minutes prior to recovery, therefore we hypothesized that the peak effect was reached during recovery phase. Findings from a specific study revealed that buprenorphine provided adequate postoperative analgesia for approximately five hours in dogs undergoing OVH.[42]

Carprofen was administered SC prior to surgical stimulation. One study showed that pre-emptive administration of carprofen was more beneficial in terms of postoperative pain control in dogs compared with postoperative administration.[26] In addition, the use of carprofen can significantly reduce wound swelling, which may further contribute to analgesia.[41] A combination of buprenorphine and carprofen has been shown to provide adequate analgesia after OVH in dogs[41,42,47] and it may be a plausible explanation for a low incidence of animals requiring rescue analgesia postoperatively.

Moreover, dogs treated with ketamine prior to surgery were found to require significantly less intervention analgesia than the control group, although plasma levels of ketamine were unlikely to be analgesic by the time surgery was completed.[43]

The pre-emptive administration of dexmedetomidine, ketamine, morphine and carprofen, as well as administration of buprenorphine, could explain the low postoperative pain scores and the overall low incidence of rescue analgesia in both groups. In addition, this combination of drugs may have masked the analgesic effect of IP and INC ropivacaine.

Despite the use of a multimodal analgesic approach, our study protocol did not provide adequate analgesia for all individuals. This highlights the importance of individualised pain assessment in the postoperative period.

Interestingly, a higher sedation score was associated with a lower DIVAS pain score. Sedated dogs may not show signs of pain, making pain assessment more difficult to interpret.[32] Visual assessments are inherently subjective[26,] and the pain scoring system DIVAS was probably not sensitive enough to assess the true level of pain in sedated dogs and it is supported by the fact that DIVAS score increased over time as dogs regained consciousness. Although DIVAS involves interaction with the animal, its unidimensional nature cannot adequately capture complex constructs such as pain and is highly observer dependent.[16,17]

Therefore, CMPS-SF was included with the aim of capturing the multidimensional pain experience.[35,38] The CMPS-SF is a behavioral composite scale for assessing acute pain in dogs.[15,38] It has shown good inter-observer correlation in post-procedural pain assessment.[12] It is reported that CMPS-SF can also be biased by sedation.[12,36] Early postoperative pain assessment with this tool may not capture the effect of sedation and should be interpreted carefully by the observer. We added a sedation score in the current study and tested its association to both pain scores used and we found no significant association between the sedation score and CMPS-SF.

It is worth noting that sedation in the early recovery period may be beneficial in reducing dysphoria. Dysphoria during the recovery period can result in patient and personnel harm and stress, destruction of anesthesia equipment, removal of IV access, and resistance to handling or restraint.[45] Some authors suggest that dysphoria may be confused with pain since both share common behaviours (Fox et al. 2000).[8]

In the the present study all dogs that received rescue analgesia based on CMPS-SF in group S showed high sedation scores (8–11/21) but were clearly responding to palpation of the wound and their CMPS-SF scores decreased shortly after rescue analgesia. We believe that the CMPS-SF was sensitive enough to detect signs of pain and the need for additional analgesic in these patients.

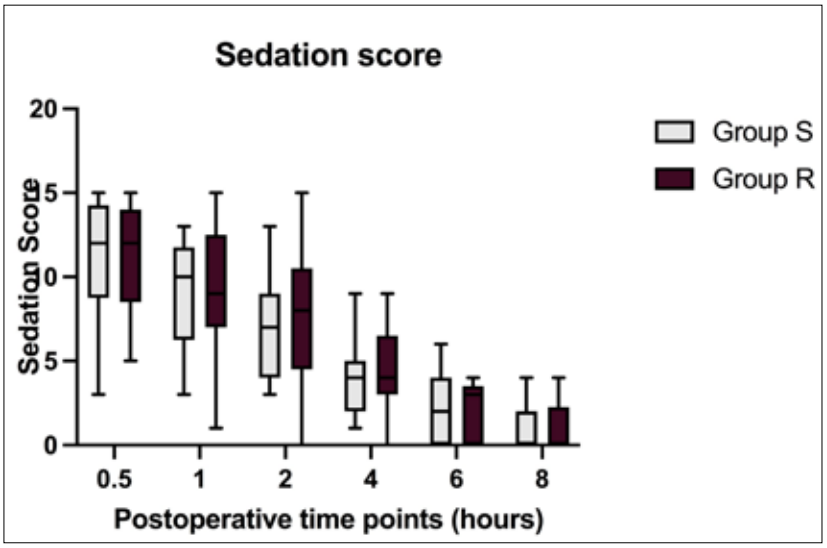

Figure 3: Box-and-whisker plots of the sedation score in 43 dogs undergoing ovariohysterectomy. Dogs received 2 mg/kg intraperitoneal and 1 mg/kg incisional ropivacaine (group R) or saline solution in same volume (group S). Dogs were evaluated from 30 minutes (T0,5) up to eight hours (T8) after extubation. Data collected after administration of rescue analgesia were not included. Each box represents the interquartile range, and the median value is the horizontal line within each box. The lower and upper whiskers represent the minimum and maximum values, respectively.

Another factor influencing the interpretation of the pain score could be the dogs' natural temperament. Most of the dogs were free roamers. Although all dogs were friendly, some of them were shy or not used to interacting with people and it is possible that this behaviour was misinterpreted as pain. On the other hand, some of the dogs may have been hiding signs of pain due to their stoic temperament. We found that some of the behavioural categories could not be applied to the study population when we used CMPS-SF and the sedation score. For example, some dogs did not respond to hand clapping even though they were fully awake. Others showed „frozen" behavior and/or an excessive response to touch due to fear or stress, which could have been mistaken for signs of pain. This raises the question of the applicability of these tools, which have been validated for pet dogs, to this specific, more feral dog population.

We found an increase of HR over time with no difference between groups. The increase in HR could be explained by the dogs' increasing activity also shown by decreasing sedation scores over time. An increase in HR could theoretically also be related to pain. The association found between RR and CMPS-SF in the current study may either be a coincidental finding or a sign that increased RR were a better indicator of pain. However, both HR and RR are considered inappropriate indicators of pain intensity in a clinical setting.[16]

The current study evaluated if the combination of INC with IP ropivacaine, as recommended by the Global Pain Council of the World Small Animal Veterinary Association, would improve postoperative analgesia by addressing both incisional and visceral pain.[34,44] The combination of IP and INC bupivacaine has been shown to provide effective analgesia compared to saline in dogs undergoing OVH. The dosage used was 4,4 mg/kg IP and a total of 15 mg INC of 0,75 % bupivacaine.[3] However, compared to 3 mg/kg IP 0,5 % bupivacaine alone, the combination of 1 mg/kg INC and 3 mg/kg IP 0,5 % bupivacaine did not show additional postoperative analgesic benefits in dogs undergoing OVH.[18] It is possible that the dose and/or concentration of the drug may have influenced these results.

The total dose of 3 mg/kg used in the current study was estimated based on previous studies on the analgesic effect of ropivacaine following IP administration of 1 or 3 mg/kg.[9,20,25] Plasma concentrations of ropivacaine have not been determined in dogs following IP administration. However, a ropivacaine dose > 4 mg/kg IV had a convulsive effect in dogs, which must be taken into account when considering higher IP dosages as the uptake via the peritoneum may be relevant.7 In humans, no signs of clinical toxicity were observed after IP instillation of ropivacaine of an average dose of 2 mg/kg, and pharmacokinetics were similar to those after extravascular administration.24 Theoretically, systemically absorbed ropivacaine could lead to sedation as occurs with lidocaine IV.28 The sedation score in the present study did not differ between groups, which makes a clinically significant effect unlikely. Therefore, 2 mg/kg IP and 1 mg/kg INC is presumably a safe dosage.

Furthermore, the inability to demonstrate an analgesic effect in the current study may be due to rapid dilution of local anaesthetics in the peritoneal cavity[40], as the efficacy of IP analgesia may be influenced by dosage, concentration, injected volume, route of administration and use of concomitant medications.[1] Based on the results of the current study it could be assumed that dosing and/or volume of distribution in the peritoneal cavity was insufficient to demonstrate additional analgesic benefit and recommendations for optimal dosing of IP ropivacaine in dogs are yet to be established.

A limitation important to mention is that inexperienced veterinary students performed the surgery, and each dog was operated by a different surgeon. Due to different surgical skills, some dogs may have suffered greater surgical trauma than others.[33] We cannot rule out that the four animals that required rescue buprenorphine suffered greater tissue trauma.

Conclusions

In the current study, the addition of 2 mg/kg ropivacaine IP and 1 mg/kg ropivacaine INC to a multimodal systemic analgesic protocol did not provide superior analgesia compared with saline. Only four of 43 dogs required rescue buprenorphine, suggesting that a multimodal analgesic protocol including dexmedetomidine, ketamine, morphine, buprenorphine and carprofen provides adequate postoperative analgesia in most animals following OVH. However, postoperative pain scoring is important to identify those individuals who require additional analgesics. Further research is needed to investigate the efficacy of IP and INC administration of ropivacaine for pain relief after visceral surgery, including different doses, volumes, and techniques.

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La ropivacaïne intrapéritonéale et incisionnelle n'améliore pas l'analgésie postopératoire lors d'une anesthésie multimodale par rapport au sérum physiologique chez des chiennes subissant une ovariohystérectomie

L'administration intrapéritonéale d'anesthésiques locaux peut réduire la douleur postopératoire après une ovariohystérectomie chez la chienne. L'objectif de cet essai clinique prospectif, randomisé, en aveugle et contrôlé par placebo était de comparer l'analgésie postopératoire et les besoins en opioïdes après l'administration intrapéritonéale et incisionnelle de ropivacaïne par rapport à du NaCl 0,9 % (sérum physiologique).

Quarante-trois chiennes appartenant à des clients ont été enrôlés dans l'étude et anesthésiés selon un protocole standardisé comprenant une prémédication par acépromazine (0,03 - 0,05 mg/kg) et dexmedetomidine (0,01 mg/kg) par voie intramusculaire. L'anesthésie a été induite avec du propofol dosé à l'effet et de la kétamine (1 mg/kg) par voie intraveineuse et maintenue avec de l'isoflurane dans de l'oxygène. Le traitement analgésique comprenait du carprofène (4 mg/kg) par voie sous-cutanée et de la morphine (0,2 mg/kg) par voie intraveineuse. En fonction de son affectation à un groupe, chaque chien a reçu soit une injection intrapéritonéale et incisionnelle de ropivacaïne (2 mg/kg et 1 mg/kg, respectivement) (groupe R), soit un volume égal de solution saline (groupe S). La buprénorphine (0,02 mg/kg) a été administrée par voie intramusculaire après l'ablation de l'utérus. La sédation et la douleur ont été évaluées 0,5, 1, 2, 4, 6 et 8 heures après l'extubation à l'aide d'une échelle de sédation, de la forme courte de l'échelle composite de douleur de Glasgow (CMPS-SF) et d'une échelle visuelle analogique interactive dynamique (DIVAS). En postopératoire, de la buprénorphine (0,01 mg/kg) a été administrée par voie intraveineuse si les chiens obtenaient un score de 6/24 sur l'échelle CMPS-SF.

Le modèle mixte ordinal n'a montré aucune différence dans les scores de douleur entre les groupes. Le test exact de Fisher n'a pas montré de différence significative dans les besoins postopératoires en buprénorphine entre le groupe S (3/22 chiens) et le groupe R (1/21 chiens) aux doses utilisées. De plus, des scores de sédation plus faibles étaient associés à des scores DIVAS plus élevés.

Dans ce protocole d'analgésie multimodale, la ropivacaïne n'a pas permis d'améliorer l'analgésie par rapport au sérum physiologique.

Mots clés: anesthésie, canine, castration, locorégionale, stérilisation, splash block

L'uso intraperitoneale e incisionale di ropivacaina non ha migliorato l'analgesia post-operatoria dopo anestesia multimodale rispetto alla soluzione salina nei cani sottoposti a ovarioisterectomia

L'amministrazione intraperitoneale di anestetici locali potrebbe ridurre il dolore post-operatorio dopo una ovarioisterectomia nei cani. Lo scopo di questo studio clinico prospettico, randomizzato, in doppio cieco, controllato con placebo, era di mettere a confronto l'analgesia post-operatoria e il fabbisogno di oppioidi dopo l'amministrazione intraperitoneale e incisionale di ropivacaina rispetto allo 0,9% di NaCl (soluzione salina).

Quarantatré cani sono stati arruolati nello studio e anestetizzati utilizzando un protocollo standardizzato che includeva la premedicazione con acepromazina (0,03 - 0,05 mg/kg) e dexmedetomidina (0,01 mg/kg) per via intramuscolare. L'anestesia è stata indotta con propofol titolato per effetto e ketamina (1 mg/kg) per via endovenosa e mantenuta con isoflurano in ossigeno. Il regime analgesico includeva carprofene (4 mg/kg) per via sottocutanea e morfina (0,2 mg/kg) per via endovenosa. A seconda dell'assegnazione al gruppo, ciascun cane ha ricevuto un'infusione intraperitoneale e incisionale di ropivacaina (rispettivamente 2 mg/kg e 1 mg/kg) (gruppo R), oppure un volume equivalente di soluzione salina (gruppo S). La buprenorfina (0,02 mg/kg) è stata somministrata per via intramuscolare una volta che l'utero è stato rimosso. Sedazione e dolore sono stati valutati 0,5, 1, 2, 4, 6 e 8 ore dopo l'estubazione utilizzando la scala di sedazione, la versione abbreviata della Glasgow Composite Pain Scale (CMPS-SF) e la scala visiva analogica interattiva dinamica (DIVAS). Dopo l'intervento, la buprenorfina (0,01 mg/kg) è stata somministrata per via endovenosa se i cani avevano un punteggio 6/24 sulla CMPS-SF.

Il modello misto ordinale non ha mostrato differenze tra i punteggi del dolore tra i gruppi. Il test esatto di Fisher non ha mostrato differenze significative nel fabbisogno post-operatorio di buprenorfina tra il gruppo S (3/22 cani) e il gruppo R (1/21 cani) alle dosi utilizzate. Inoltre, punteggi di sedazione più bassi erano associati a punteggi più alti per la DIVAS.

In questo protocollo di analgesia multimodale, la ropivacaina non è riuscita a migliorare l'analgesia rispetto alla soluzione salina.

Parole chiave: anestesia, cane, castrazione, loco, ovarioisterectomia, blocco splash

Intraperitoneal and incisional ropivacaine did not improve postoperative analgesia after multimodal anaesthesia compared with saline in dogs undergoing ovariohysterectomy

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