Combination of magnesium sulphate and ropivacaine epidural analgesia for hip arthroplasty in dogs

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Cover Letter

Elena Lardone: student and main investigator of the project. Data collection, data management, preparation of the manuscript.

Bruno Peirone: experienced orthopaedic surgeon who performed hip arthroplasty in all dogs involved in the study. Supervision of data collection, manuscript correction.

Chiara Adami: senior researcher and scientific director of the project. Design, data interpretation, statistical analysis, correction of the manuscript.

Title page

Combination of magnesium sulphate and ropivacaine for lumbo-sacral epidural analgesia in dogs undergoing hip arthroplasty: an investigator-blind, randomized, prospective clinical trial

Elena Lardone[*], Bruno Peirone[*] & Chiara Adami[†]

[*]*Department of Veterinary Science, University of Torino, Grugliasco, Torino, Italy*

[†]*Department of Clinical Sciences and Services, Royal Veterinary College, University of London, Hawkshead Campus, North Mymms, AL97TA Hatfield, UK*

Correspondence: Elena Lardone, Department of Veterinary Science, University of Torino, Grugliasco, Torino, Italy, 10095

E-mail: elena.lardone@unito.it

Tel.: +39 0116709061

Fax: +39 0116709061

Running head: $MgSO_4$ for epidural analgesia in dogs

Abstract

Objective

The aim of this investigator-blind, randomized, prospective clinical trial was to investigate whether the magnesium sulphate added to ropivacaine via epidural route would provide prolonged and better perioperative analgesia without effects on the duration of motor block and on the hind limbs neurological function.

Study design

The study has been designed as an investigator-blind, controlled, randomized, prospective clinical trial.

Animals

Twenty client-owned dogs undergoing hip arthroplasty were randomly allocated to one of two treatment groups: group C (control, receiving 1 mg kg^{-1} epidural ropivacaine) or group M (magnesium, receiving a mixture of 1 mg kg^{-1} ropivacaine and 2 mg kg^{-1} magnesium sulphate by epidural route).

Methods

Intraoperatively, nociception was assessed on the basis of changes in respiratory rate, heart rate and mean blood pressure above baseline values. Postoperatively, the same observer evaluated the pain with a modified Sammarco pain score, a Glasgow pain scale and a visual analogue scale. A modified Tarlov scale was used to assess motor block. All dogs were evaluated at recovery and then 1, 2, 3, 4, 5 and 24 hours after that. Rescue analgesia was provided during surgery with fentanyl and, postoperatively, with buprenorphine.

Results

The two treatment groups did not differ with respect to intra-operative physiological variables, rescue analgesics requirement, post-operative pain scores and duration of motor block.

Conclusions and clinical relevance

The addition of epidural magnesium to ropivacaine did not improve, neither did it prolong, the peri-operative analgesia provided by ropivacaine alone. Further studies are needed to determine whether an epidural magnesium dose higher than 2 mg kg^{-1} would exert a more pronounced analgesic effect, without prolonging the duration of the motor block, in dogs undergoing hip arthroplasty.

Keywords: Analgesia; Dog; Magnesium Sulphate; Ropivacaine; Epidural anaesthesia

Introduction

Total hip replacement is an innovative and complicated procedure used in dogs to treat hip dysplasia and other pathological conditions affecting the coxofemoral joint. As hip arthroplasty is an invasive technique, dogs undergoing this kind of surgery may experience severe pain. Providing adequate perioperative analgesia during invasive orthopaedic surgeries not only is an ethical obligation for the veterinarian, but also plays a crucial role in the outcome of the surgery itself (Conzemius et al. 2005). Indeed, effective prevention and treatment of pain has been shown to significantly improve patient's attitude, as well as limb's use and function (Conzemius et al. 2005).

As an alternative to systemic analgesia, loco-regional anaesthetic techniques offer the advantage of a selective and targeted block of the anatomical area of interest. Among neuroaxial techniques, epidural administration of analgesics is traditionally regarded as safer as and easier to perform than the spinal route. Owing to its popularity, practicality and ease of performance, single epidural injection is usually preferred to constant rate infusion of analgesics via this route, which can only be accomplished after insertion of an epidural catheter. Placing an epidural catheter is a time-consuming procedure, which requires a certain degree of expertise and also carries the risk of complications (Ladha et al. 2013; Pumberger et al. 2013). On the other hand, single epidural injections may provide analgesia of insufficient duration when invasive and potentially long surgeries are performed.

Within the last twenty years, there has been an increasing interest to multimodal approach to pain in veterinary patients, especially with respect to the use of agents which, without being classified as analgesic, do have antinociceptive properties (Kukanich 2013; Madden et al. 2014; Crociolli et al. 2015; Norkus et al. 2015). Among these, magnesium plays a central role in the prevention of central sensitization by blocking the dorsal horn NMDA (N-methyl-D-aspartate) receptors in a non-competitive, voltage dependent fashion. Magnesium sulphate is inexpensive, stable at room temperature and available in Europe with a formulation whose use is approved for dogs. The neurotoxicity of intrathecal magnesium sulphate was studied in dogs and neither neurological deficits nor histopathological changes in the spinal cord were found after a dose of 3 mg kg^{-1} (Simpson et al. 1994). The studies investigating the clinical role of magnesium as adjuvant in pain therapy show conflicting results. Intravenous magnesium failed in treating perioperative pain in both humans and dogs (Murphy et al. 2013; Rioja et al. 2012). On the other hand, several clinical trials showed that magnesium effectively improves analgesia in human patients receiving combinations of local anaesthetics and opioids, by either epidural or spinal route (Buvanendran et al. 2002; Oezalevli et al. 2005; Arcioni et al. 2007). The nociceptive effects of magnesium were demonstrated experimentally in dogs (Bahrenberg et al. 2015), however there is a paucity of data regarding the clinical use of magnesium in this species. A clinical trial suggests that the addition of spinal magnesium sulphate to ropivacaine increases the duration and the intensity of analgesia, but also of the motor block, provided by ropivacaine alone in dogs undergoing orthopaedic surgery (Adami et al. 2016).

The aim of this study was to determine whether the addition of magnesium sulphate to epidural ropivacaine would result in better peri-operative analgesia - in terms of longer duration and decreased need for rescue analgesics - than ropivacaine alone, in client-owned dogs undergoing elective hip arthroplasty.

Our hypothesis was that the addition of magnesium to ropivacaine would improve peri-operative analgesia, without prolonging the duration of the motor block or causing neurological dysfunction of the hind limbs.

Materials and methods

Animals

Twenty client-owned dogs undergoing elective hip arthroplasty between March 2014 and February 2016 were involved in this study. All dogs underwent a pre-anaesthetic physical examination and a complete blood test, including haematology and biochemistry, was carried out to rule out abnormalities. Exclusion criteria were ASA (American Society of Anaesthesiologists) risk category higher than II and skin infections at the level of the lumbosacral area. The clinical trial was performed with permission of the Ethical Committee of the Veterinary Teaching Hospital of the University of Turin (Italy), and written informed owner consent.

Study design

This study was designed as an investigator-blind, controlled, randomized, prospective clinical trial. A block randomization method was used in order to allocate the dogs to one

of two treatment groups. Briefly, an operator not involved in the study was in charge for keeping an opaque, sealed envelope from which treatment assignments were shuffled and drawn. This same operator was also responsible for the allocations' list, which was disclosed only at the end of the trial. The number of dogs per group was determined on the basis of a sample size calculation. Each group was to be composed of a minimum of 10 dogs in order to detect, with one way analysis of variance (with power equal to 0. 95% level of confidence and α value and standard deviation set at 0.05 and 40 minutes, respectively), a difference between groups in the mean duration of analgesia (defined as the time elapsed from the epidural injection to the first administration of rescue analgesics) equal to at least 60 minutes.

Anaesthetic protocol and procedures

All dogs were premedicated with intramuscular (IM) acepromazine (0,03 mg kg^{-1}, Prequillan; Fatro, Italy). Thereafter, intravenous (IV) propofol (Vetofol; Esteve, Spain) was titrated to effect to induce general anaesthesia. After orotracheal intubation, isoflurane (Isoflo; Esteve, Spain) was delivered in oxygen via a circle system and lactated Ringer's solution was perfused IV (10 mL kg^{-1} hr^{-1}, Ringer Lattato; Fresenius Kabi, Italy). Systolic (SAP), mean (MAP) and diastolic (DAP) blood pressures were continuously measured through an indwelling catheter placed in the dorsal pedal artery. Monitoring during anaesthesia included both cardiovascular (SAP, MAP, DAP, heart rate [HR] and rhythm) and respiratory (end tidal carbon dioxide [$P_E'CO_2$], peak inspiratory pressure [PIP], respiratory rate [f_R], tidal volume [V_T], minute volume [V_E], inspired fraction of oxygen [FiO_2], end tidal isoflurane tension [$P_E'_{ISO}$]) parameters, as well as oesophageal

temperature (T°,C). Manual data recording was performed every 5 minutes for the entire duration of anaesthesia. Spontaneous breathing was preferred unless $P_E'CO_2$ reached more than 45 mmHg; in that case mechanical ventilation was used to maintain normocapnia. During anaesthesia the target was a constant $P_E'_{ISO}$ of 1.3%, equivalent to the Minimum Alveolar Concentration (MAC) for the dog (Steffey & Mama 2007).

A bolus of IV atropine (0.01 mg kg^{-1}, Atropina Solfato; ATI, Italy) was injected when bradycardia (<45 beats per min [BPM]) occurred. Treatment of hypotension (MAP <60 mmHg) consisted of an IV bolus of lactated Ringer's solution (10 mg kg^{-1} over 10 min), followed by an IV colloid bolus (Voluven; Fresenius Kabi, Italy; 2 mL kg^{-1} over 10 minutes), and then by an IV infusion of dopamine (Revivan; AstraZeneca, Italy; starting at 10 μg kg^{-1} min^{-1}, to be incremented by 2.5 μg kg^{-1} min^{-1} every 10 min until MAP increased above 60 mmHg) in the event of unresponsive hypotension. Cardiac bradyarrhythmias and persistent hypotension were regarded as clinical symptoms compatible with hypermagnesaemia and their occurrence was recorded. The duration of surgery and of anaesthesia (minutes) were recorded. The time elapsed from termination of inhalational anaesthesia to recovery to intensive care unit (minutes) was defined as "time to recovery", and recorded. After tracheal extubation, all dogs received IV carprofen (4 mg kg^{-1}, Rimadyl; Pfizer, Italy). The dogs were discharged 24 hours after surgery.

Epidural injection

As soon as the anaesthesia plane was judged adequate on the basis of classical clinical parameters (jaw relaxation, absence of active blinking and light or absent palpebral reflex, immobility and physiological parameters within normal ranges for the species) the anaesthesist (**), who was blinded to the treatment, performed all the epidural injections. The dogs were positioned in sternal recumbency with the hind limbs forwarded symmetrically in order to maximize the dorsal lumbosacral space. The ilium wings, together with the sacrum and the dorsal spinous processes of L6 and L7, were used as anatomical landmarks. After surgical preparation of the area, a 75 mm, 19 gauge spinal needle was inserted percutaneously between L7 and S1, with the bevel facing cranial, and then forwarded through the intervertebral ligament into the epidural space. Both the "popping" sensation, perceived while penetrating the interarcuate ligament, and the hanging drop technique were used for a first assessment of proper needle placement. Radiographic exam followed to confirm correct positioning of the needle between L7 and S1.

Treatment groups

Epidural ropivacaine (Naropina 0.5%; AstraZeneca, Italy) at the dose of 1 mg kg^{-1} (equivalent to a volume of 0.2 mL kg^{-1}), was administered epidurally to group C (Control), while group M (Magnesium) received a mixture of ropivacaine (1 mg kg^{-1}) and magnesium sulfate (Magnesio Solfato 2g 10mL^{-1}; Galenica Senese, Italy) at the dose of 2 mg kg^{-1} (equivalent to a volume of 0.01 mL kg^{-1}). The drugs were given as a single bolus over 1 minute. Doses were chosen on the basis of the authors' past clinical

experience, and of human and veterinary medicine literature (Arcioni et al. 2007; Bilir et al. 2007; Oezalevli et al. 2005).

Assessment of intra-operative nociception and post-operative pain

Intraoperative nociception was defined as any increase in HR, MAP and/or f_R of 20% above baseline values (recorded before skin incision, after $P_E{'}_{ISO}$ had been maintained constant at 1.3% for at least three consecutive measurements, over 15 min). When two of these three parameters increased above the defined values, rescue fentanyl (Fentanest; Pfizer, Italy) was administered IV (0.003 mg kg^{-1}).

Postoperatively, a modified multifactorial pain score (Table 1) (Sammarco et al. 1996; Adami et al. 2012) and the Glasgow pain scale (Holton et al. 2001) were used to evaluate pain. Besides, a 100 mm visual analogue scale (VAS) with end points labelled "worst pain imaginable" (0) and "no pain" (10) was utilized. Rescue analgesia consisted of IV buprenorphine (Temgesic; Schering Plough, UK), 0.01 mg kg^{-1}, given when one or more pain scores exceeded 40% of the maximum value of the scale (>4 for the VAS, >5 for the multifactorial pain score scale, >8 for the Glasgow pain scale). Neurological assessments were based on a modified Tarlov's scale (Table 2) (Buvanendran et al. 2002; Adami et al. 2016) in order to evaluate the neurological function of the hind limbs and the degree of motor blockade. The same observer (**), who was unaware of the treatment, performed all the evaluations. All dogs were evaluated as soon as they were awake enough to respond to stimulation (vocal call and incitement to sit or stand up) and then 60, 120, 180, 240, 300 minutes and 24 hours after surgery.

Statistics

Commercially available software (SigmaStat and SigmaPlot 12, Systat Software Inc.) were used for statistical analysis. Normality of data distribution was assessed with the Kolmogorov-Smirnov test and with the Shapiro-Wilk test. Following, continuous variables were analysed with either one way repeated measures analysis of variance followed by Holm-Sidak method for multiple comparison, or Friedman repeated measures analysis of variance on ranks followed by Tukey test, where it applied. For the analysis of intra-operative cardiovascular and respiratory variables, only the values recorded at three different time points were used: prior to surgical stimulation (baseline as above described: 0), immediately after skin incision (1), and immediately after the beginning of tibial osteotomy (2).

For non-continuous variables, either T-test or Mann Whitney Rank Sum test were used. The proportions of dogs within each treatment group in which hypotension and bradyarrhythmias were observed following epidural injection of magnesium were analysed with the Fisher exact test. P values < 0.05 were considered statistically significant.

Results

Data are presented as either means ± SD or medians [25%-75% ranges].

Heart rate, MAP, time to recovery and duration of anaesthesia were normally distributed. Anaesthesia was uneventful in all dogs enrolled in the study and lasted 222 ± 62 minutes in group M and 220 ± 32 minutes in group C, respectively; this difference was not statistically significant. The treatment groups did not differ with respect to intra-operative physiological variables (Figure 1). However, HR decreased over time in the control group, while MAP increased in both treatment groups. Respiratory rate increased over time in group M while it decreased in group C. Cardiovascular events compatible with hypermagnesaemia, namely bradyarrhythmias and hypotension, were not observed during the anaesthetics. Three dogs of group M (0[0-1]) and 4 of group C (0[0-2]) needed boluses of rescue fentanyl during surgery. This difference was not statistically significant. No difference in duration of surgery, which lasted 120 [90-120] and 125 [120-150] minutes in groups M and C, respectively, was detected between groups. Only one dog, assigned to the control group, needed rescue buprenorphine before completion of pain assessments.

The control group achieved lower VAS scores (9.2[7.5-10] versus 9.5[7.9-10]) and higher Sammarco and Glasgow scores (1[0-3] versus 1[0-2.75] and 2[1-3] versus 1[1-4], respectively) than group M at the majority of the time points, however these differences were not statistically significant (Figure 2; Table 3). Group M had lower scores for the Tarlov's scale than group C (2[0-4] versus 3[0-4]) but this difference was not significant. In both groups the Sammarco, the Glasgow and the Tarlov's scores significantly increased over time, while VAS decreased.

Recovery was smooth in all the dogs included in the study and normal motor function of the hind limbs was recovered within 6 hours from the epidural injection. Peri-anaesthetic complications were not observed.

Discussion

Although the addition of epidural magnesium to ropivacaine resulted in less rescue analgesics requirement and lower post-operative pain scores and higher VAS compared to ropivacaine alone, we failed in demonstrating a statistically significant difference in terms of quality and duration of analgesia between the two treatments. The duration of the motor block was also comparable between the two groups, and the administration of magnesium was not associated to neurological dysfunction of the hind limbs.

Our findings are in disagreement with those of a previous study, which found that the spinal addition of magnesium to ropivacaine potentiated the intensity and the duration of peri-operative analgesia in dogs undergoing tibial plateau levelling osteotomy (Adami et al. 2016), but also prolonged the duration of the motor block.

Possible explanations for this discrepancy are less effective analgesia when magnesium is given epidurally compared to the spinal route or, alternatively, a failure in the methods used in the current study to detect a difference between treatments.

Besides the possibility of a direct analgesic effect of magnesium on the dorsal horn NMDA receptors, Adami and colleagues hypothesized that the ionized magnesium released by its salt could exert antinociception also by altering the resting potential of the

neuronal membranes through a blockade of the calcium currents (Adami et al. 2016). Alternatively, as a hyperosmolar salt, magnesium sulfate might affect the osmotic homeostasis of cerebrospinal fluid and spinal cord, leading to axonal shrinking and transient neurologic dysfunction (Adami et al. 2016). Both mechanisms are more likely to occur when magnesium is injected spinally rather than via the epidural route, owing to a more direct contact with the cerebrospinal fluid and the spinal cord.

Another possible explanation is that the epidural route of administration requires a higher magnesium dose than the spinal one in order to detect appreciable analgesia. Owing to ethical obligations, and not to cause any harm to client-owned dogs, in the current study it was decided to use a dose of magnesium which was proven to be safe in terms of risks for direct neurotoxicity (Simpson et al. 1994) and hypermagnesaemia (Adami et al. 2016). Nonetheless it cannot be excluded that a higher magnesium sulfate dose might have resulted in more pronounced clinical effects.

Pain assessment in non-verbal patients might be extraordinarily challenging even for experienced observers, especially when subjective indicators, namely behavioural signs of pain, are evaluated (Conzemius et al. 1997; Reid et al. 2007). The choice of having one single investigator in charge for all the assessments, as well as of using several pain scales instead of one, should have overcome some potential intrinsic limitations, namely the inter-observer variability and poor sensitivity and specificity of the scale used to evaluate pain.

Another potential limitation of this study is the absence of an unconfutable proof that the needle had been correctly placed within the epidural space in all dogs. Although the

hanging drop technique was used to guide needle's insertion, and radiography to verify the needles' position within the targeted intervertebral space, only an epidurography, accomplished with the injection of a contrast medium, would have inarguably confirmed that the tip of the needles had reached the adequate depth. Due to ethical considerations regarding to client-owner dogs, the use of invasive or potentially harmful techniques for this purpose could not be considered. Failure in identifying the exact injection site would have distorted the results; however, the requirement of no or little rescue analgesia, together with the detection of motor block in all dogs at recovery, suggests that the epidural injections were correctly performed.

Assuming that all the injections had been performed within the epidural space, an alternative possible explanation for the lack of differences between the two treatments is that ropivacaine alone, at the dose and concentration used in the current study, might already be adequate as analgesic treatment for hip replacement. In this scenario, detecting an appreciable difference would be more challenging and possibly require a larger sample size. Unfortunately, the use of a suboptimal analgesic treatment instead of ropivacaine would have raised some ethical concerns and was for this reason regarded as an unsuitable option.

In the dogs enrolled in the current study plasma magnesium concentrations were not measured. Although 2 mg kg^{-1} of spinal magnesium sulphate were found not to significantly increase total plasma magnesium concentrations in dogs (Adami et al. 2016), it cannot be assumed that the same dose administered epidurally would have similar uptake and redistribution. As a consequence, mild hypermagnesaemia might have gone

undetected in the dogs enrolled in the current study. However, it is reasonable to assume that a clinically relevant hypermagnesaemia would have been accompanied by cardiac arrhythmias and, possibly, persistent hypotension, none of which was not noticed in the study population.

Conclusions

In conclusion, the addition of 2 mg kg^{-1} magnesium sulphate to epidural ropivacaine did not result in considerable improvement of quality and duration of peri-operative analgesia, but neither prolonged the motor block. Further trials are needed to determine whether a higher dose of magnesium administered via the epidural route would increase the analgesic effect in dogs undergoing orthopaedic surgery.

Conflict of interest statement

None of the authors have financial or personal relationships with individuals or organisations that could inappropriately influence or bias the content of the paper.

References

-Adami C, Casoni D, Spadavecchia C et al. (2016) Addition of magnesium sulphate to ropivacaine for spinal analgesia in dogs undergoing tibial plateau levelling osteotomy. Vet J. 209, 163-168.

-Adami C, Veres-Nyéki K, Bergadano A et al. (2012) Evaluaton of peri-operative epidural analgesia with ropivacaine, ropivacaine and sufentanil, and ropivacaine, sufentanil and epinephrine in isoflurane anesthetized dogs undergoing tibial plateau levelling osteotomy. Vet J. 194, 229-234.

-Arcioni R, Palmisani S, Tigano S (2007) Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: A prospective, randomized, double-blind, controlled trial in patients undergoing major orthopaedic surgery. Acta Anaesthesiol Scand 51, 482-489.

-Bahrenberg A, Dzikiti BT, Rioja E et al. (2015) Antinociceptive effects of epidural magnesium sulphate alone and in combination with morphine in dogs. Vet Anaesth Analg 42, 319-328.

-Bilir A, Gulec S, Ozcelik A et al. (2007) Epidural magnesium reduces postoperative analgesic requirement. Br J Anaesth 98, 519-523.

-Buvanendran A, McCarthy R, Tuman KJ at al. (2002) Intrathecal magnesium prolongs fentanyl analgesia: A prospective, randomized, controlled trial. Anesth Analg 95, 661-666.

-Conzemius M, Evans R, Wagner S et al. (2005) Effect of surgical technique on limb function after rupture of the cranial cruciate ligament in dogs. J Am Vet Med Assoc 226, 232-236.

-Conzemius M, Hill C, Perkowski S et al. (1997) Correlation between subjective and objective measures used to determine severity of postoperative pain in dogs. J Am Vet Med Assoc 210, 1619-162.

-Crociolli GC, Cassu RN, Nicácio GM et al. (2015) Gabapentin as an adjuvant for postoperative pain management in dogs undergoing mastectomy. J Vet Med Sci 77, 1011-1015.

-Holton L, Reid J, Nolan A et al. (2001) Development of a behaviour-based scale to measure acute pain in dogs. Vet Rec 148, 525-531.

-KuKanich B (2013) Outpatient oral analgesics in dogs and cats beyond nonsteroidal anti-inflammatory drugs: An evidence-based approach. Vet Clin North Am Small Anim Pract 43, 1109-1125.

-Ladha A, Alam A, Idestrup, Chol S et al. (2013) Spinal haematoma after removal of a thoracic epidural catheter in a patient with coagulopathy resulting from unexpected vitamin K deficiency. Anaesth 68, 856-860.

-Madden M, Gurney M, Bright S (2014) Amantadine, an N-Methyl-D-Aspartate antagonist, for treatment of chronic neuropathic pain in a dog. Vet Anaesth Analg 41, 440-441.

-Murphy J, Paskaradevan J, Wu C et al. (2013) Analgesic efficacy of continuous intravenous magnesium infusion as an adjuvant to morphine for postoperative analgesia: a systematic review and meta-analysis. Middle East J Anaesthesiol 22, 11-20.

-Norkus C, Rankin D, KuuKanich B et al. (2015) Pharmacokinetics of oral amantadine in greyhound dogs. J Vet Pharmacol Ther 38, 305-308.

-Oezalevli M, Cetin T, Isik G et al. (2005) The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anaesthesia. Acta Anaesthesiol Scand 49, 1514-1519.

-Pumberger M, Memtsoudis S, Hughes A et a. (2013) An analysis of the safety of epidural and spinal neuraxial anesthesia in more than 100,000 consecutive major lower extremity joint replacements. Reg Anesth Pain Med 38, 515-519.

-Reid J, Nolan AM, Scott EM et al. (2007) Development of the short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score. Animal Welfare 16, 97-104.

-Rioja E, Dzikiti B, Schoeman JP (2012) Effects of a costant rate infusion of magnesium sulphate in healthy dogs anaesthetized with isoflurane and undergoing ovariohysterectomy. Vet Anaesth Analg 39, 599-610.

-Sammarco J, Conzemius M, Smith GK et al. (1996) Postoperative analgesia for stifle surgery: A comparison of intra-articular bupivacaine, morphine, or saline. Vet Surg 25, 59-69.

-Simpson J, Eide T, Koski G et al. (1994) Intrathecal magnesium sulfate protects the spinal cord from ischemic injury during thoracic aortic cross-clamping. Anesthesiol 81, 1493-1499.

Steffey E, Mama K (2007) III Pharmacology. In: Lumb and Jones'Veterinary Anesthesia and Analgesia. Tranquilli, W., Thurmon, J., Grimm, K. (eds).

Figure legends

Fig.1. Intra-operative physiological variables recorded from 20 dogs anaesthetized for THR and assigned to one of two treatment groups: group C (Control, received epidural ropivacaine; n=10) and group M (Magnesium, received an epidural combination of magnesium and ropivacaine; n=10). 0: values recorded as baseline in the anaesthetized dogs prior to surgical stimulation; 1: values recorded immediately after skin incision; 2: values recorded after tibial osteotomy; *: statistically significant difference between time points and the baseline.

Fig.2 Post-operative pain scores recorded from 20 dogs anaesthetized for THR and assigned to one of two treatment groups: group C (Control, received epidural ropivacaine; n=10) and group M (Magnesium, received an epidural combination of magnesium and ropivacaine; n=10). 1: values recorded after recovery, as soon as the patients were able to sit and respond to vocal call; 2, 3, 4, 5 and 6 are 60, 120, 180, 240, 300 minutes and 24 hours after recovery; *: statistically significant difference between time points and the baseline.

Table 1

Modified multifactorial pain score (Sammarco et.al., 1996; Adami et al., 2012) to assess post-operative pain in 20 dogs undergoing total hip replacement.
The same observer who was blind to the treatment evaluated the dogs as soon as they were awake enough to respond to stimulation (vocal call and incitement to sit or stand up) and then 60, 120, 180, 240, 300 minutes and 24 hours after surgery.

Vocalization -None -Intermittent vocalization -Continuous vocalization	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2
Movement -None -Frequent position changes - Rolling, thrashing	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2	0 1 2
Agitation -Calm -Mild agitation -Moderate agitation -Severe agitation	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3
Heart rate -1-15% above pre-operative value -16-29% above pre-operative value -30-45% above pre-operative value ->45% above pre-operative value	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3
Respiratory rate -1-15% above pre-operative value -16-29% above pre-operative value -30-45% above pre-operative value ->45% above pre-operative value	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3	0 1 2 3

Total (0-13)								

Table 2

Modified Tarlov's scale (Buvanendran et al., 2002; Adami et al., 2016) to evaluate the neurological function of the hind limbs and the degree of motor blockade in 20 dogs undergoing total hip replacement.

The same observer who was blind to the treatment evaluated the dogs as soon as they were awake enough to respond to stimulation (vocal call and incitement to sit or stand up) and then 60, 120, 180, 240, 300 minutes and 24 hours after surgery.

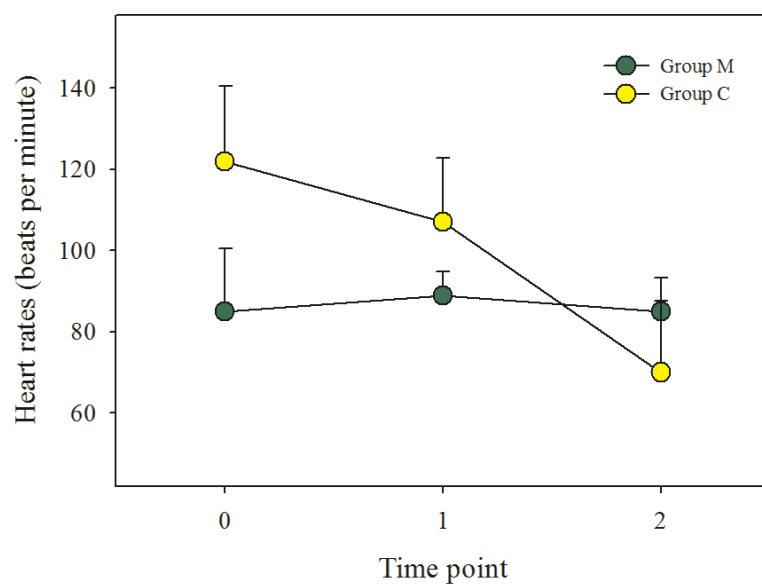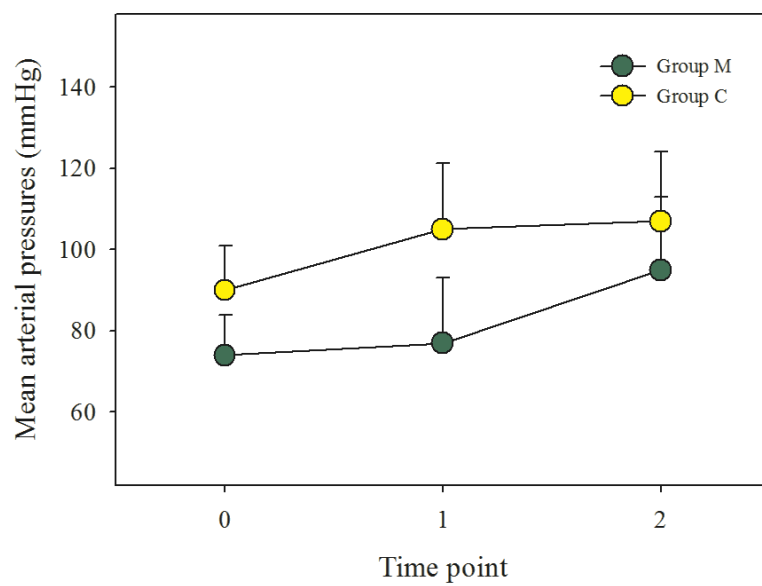| Grade 0	Flaccid paraplegia, no movements of the hind limbs, possible loss of bowel/ urinary bladder control
Grade 1	Spastic paraplegia with moderate or vigorous purposeless movements of the hind limbs. No sitting, unable to walk
Grade 2	Good movements of the hind limbs but unable to stand
Grade 3	Able to stand but unable to walk normally; hips and limbs obviously unstable, moderate to severe ataxia
Grade 4	Able to stand and walk normally, some muscle weakness of the hind limbs may be seen

Table 3

P and q values of intra-operative and post-operative variables recorded from 20 dogs undergoing hip arthroplasty and assigned to either group C (Control, received epidural ropivacaine; n=10 dogs) or group M (Magnesium, received an epidural combination of magnesium and ropivacaine; n=10 dogs). NA: not applicable.

VARIABLE	P value	q value
DURATION OF ANAESTHESIA Group M versus Group C	0.87	NA
REQUIREMENT OF RESCUE FENTANYL Group M versus Group C	0.42	NA
DURATION OF SURGERY Group M versus Group C	0.19	NA
HEART RATE Group M versus Group C Group M versus time Group C versus time	0.050 0.025 0.017	NA NA NA

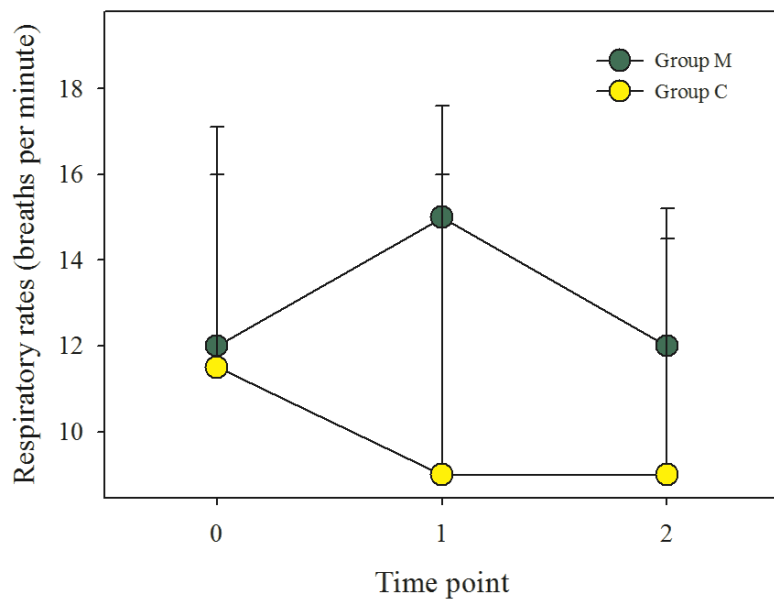| MEAN ARTERIAL PRESSURE		
Group M versus Group C	>0.05	1.10
Group M versus time	<0.05	8.80
Group C versus time	<0.05	7.70
RESPIRATORY RATE		
Group M versus Group C	>0.05	0.36
Group M versus time	<0.05	8.00
Group C versus time	<0.05	8.40
SAMMARCO SCORE		
Group M versus Group C	>0.05	1.00
Group M versus time	<0.05	6.00
Group C versus time	<0.05	5.00
GLASGOW SCORE		
Group M versus Group C	>0.05	3.10
Group M versus time	>0.05	2.80
Group C versus time	>0.05	0.30
VAS SCORE		
Group M versus Group C	>0.05	0.50
Group M versus time	<0.05	12.16
Group C versus time	<0.05	11.65
TARLOV'S SCORE		
Group M versus Group C	>0.05	2.40
Group M versus time	<0.05	6.80
Group C versus time	<0.05	4.60

Figure 1

Figure 2