EVALUATION OF EPIDURAL ANESTHESIA WITH LIDOCAIN COMPARED TO BUPRENORPHINE AND THE COMBINATION OF LIDOCAIN - BUPRENORPHINE IN DOGS

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Abstract

The aim of our study is the comparative evaluation of epidural anesthesia by determining the antinociceptive efficacy and the modification of cardiorespiratory variables, in dogs in which a local anesthetic (lidocaine) and an opioid analgesic (buprenorphine) were injected into the epidural space separately and in combination. The solutions were administered in the epidural space to the dog as follows: lidocaine 2% (2.5 mg / kg) and buprenorphine (concentration to be added) (1.5 mcg/kg), respectively lidocaine 2% (5 mg/kc) or buprenorphine 0.3 mg/ml (3 mcg/kc). Lidocaine had excellent penetrability, rapidly producing onset (1.7 ± 0.30 min.) and onset of surgical anesthesia. However, it did not induce long-lasting sensory and motor nerve block and no satisfactory analgesia (6.0 ± 0.1.). Buprenorphine had a slow onset, but with a long-lasting analgesic effect (108.0 ± 41.6 min.). Epidural administration of opioids provides additional intra- and postoperative analgesia, in which case buprenorphine may be the drug of choice in laborious surgical procedures**.**

Key words: epidural anesthesia, lidocaine, buprenorphine, analgesia

INTRODUCTION

Preoperative epidural injection of local anesthetics and opioids provides excellent preemptive, multimodal intraoperative analgesia, reduces the concentration of volatile anesthetic required to maintain surgical anesthesia, and provides analgesia extending into the recovery period. Epidural administration of drugs for pain management has been widely used in veterinary medicine (*Jones RS., 2001; Steagall PVM et al., 2017*).

The lumbosacral intervertebral space is the most common location for epidural injection in small animals. Epidural administration of local anesthetics provides complete anesthesia, sufficient to perform surgery, to the caudal half of the body. Administering opioids epidurally provides additional analgesia often of longer duration and with fewer adverse effects than systemic administration. Lumbosacral epidural anesthesia with local anesthetics provides complete anesthesia to the caudal half of the body by blocking the intradural spinal nerve roots and the peripheral layer of the spinal cord (*Stoelting RK, Hillier SC, 2006*). This technique is useful for pelvic and hindlimb orthopedic procedures, perineal and anal surgeries, exploratory laparotomy, and cesarean section. In addition to complete anesthesia, at least some sympathetic and motor blockade is produced with local anesthetics. Lidocaine, mepivacaine, and bupivacaine consistently cause motor blockade, while motor blockade is less intense and of shorter duration with levobupivacaine and ropivacaine (*Stoelting RK, Hillier SC, 2006*). The duration of motor blockade is generally shorter than the duration of analgesia, and, depending on the procedure and local anesthetic chosen, motor function usually returns by the time a patient recovers from anesthesia (*Lemke KA., 2007*; *Scarda RT, Tranquilli WJ*., 2007; Stoelting RK, Hillier SC, 2006).

MATERIAL AND METHOD

The study was performed on 15 healthy common breed dogs (13 males and 2 neutered females). They weighed an average of 10.8 ± 1.4 kg and were kept in identical conditions during the experiment. The dogs received water ad libidum (at discretion), and 12 hours before the experiment they were stopped feeding. Also, before starting the experiment, they underwent a rigorous physical and biochemical examination. The commercial products used were: Lidocaine®, 2% solution with 1: 200,000 epinefrine in 20 ml vials and Bupaq, 0.3 mg / ml (0.003%) solution.

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A catheter was inserted into the antebrachial cephalic vein to collect blood samples to determine blood gas, arterial and venous pH (pHa, pHv), concentration in arterial and venous hemoglobin (Hg, g/dl), and others parameters using the AVL Compact 2 gas analyzer. A non-invasive indirect automatic device (Digital Electronic Blood Pressure Monitor, Model FC - 150 D, Tokyo, Japan) was used to measure blood pressure and heart rate. Respiratory rate was assessed by observing and counting chest "trips". Rectal temperature was measured in degrees Celsius (0C), using an electronic thermometer (Termir® 4 Electronic Veterinary Thermometer).

The dogs did not receive water and food 6 hours before the anesthesia. They were placed in lateral decubitus, after being pre-anesthetized with acepromazine, 1% solution - 0.5 mg / kc, i.m., in ventroflexion to highlight the lumbar vertebral space. The craniodorsal iliac spine, the dorsal spinal process of the L7 vertebra and the median sacral ridge were palpated. Asepsis followed the rules of any surgical procedure (the lumbosacral region was trimmed, shaved and aseptically prepared for each dog).

Experimental Design: the puncture needle (i.v. catheter 18GA 1.77IN - 1.3 x 45 mm) is inserted in the center of the lumbosacral space perpendicular to the midline of the kidney and in a strictly sagittal plane, using the left index as a guide. The catheter is inserted 1 - 1.5 cm, and after the needle is withdrawn, a syringe with 7 ml of sterile isotonic saline (0.9% NaCl) is attached to the cannula to tactilely assess the resistance during the progression of the needle. enlarges suddenly when the needle penetrates the yellow ligament. After an advance of a few millimeters, a sudden loss of resistance indicates penetration into the epidural space. The injection of the solutions into the epidural space was done slowly over a period of at least 30 seconds.

Each dog was randomly given 3 treatments: lidocaine (5 mg/kg), bupivacaine (3 mcg/kg) and a combination of the two in a half dose: lidocaine (2.5 mg/kg) and bupivacaine (1.5 mcg/kg). A time interval of at least 14 days was observed between administrations, each anesthetic being appropriately diluted with an injection volume of 3 ml with isotonic saline. The installation of sensory blockage (analgesia) was assessed by the response to the pressure applied on the digital perineum, perineum and flanks with a hemostatic forceps (closed at the first teeth). The initiation and installation of motor blockage was appreciated by the feeling of general weakness or by the inability of the dog to carry the weight of its hind limbs, the absence of skeletal muscle tone.

Lateral decubitus time, onset of analgesia, duration of analgesia, and recovery time from anesthesia (sternal decubitus period) were measured for each dog. Heart rate, mean blood pressure, respiratory rate, rectal temperature, and blood biochemical tests were measured before the epidural injection and then at 15-minute intervals for a 75-minute post-injection period.

Data are presented as M ± DS. Anesthetic indices were compared using the Student's test. The ANOVA test (analysis of variance) was used to compare measurements of physiological indices: heart rate, respiratory rate, mean blood pressure, rectal temperature and blood biochemical indices. For all analyzes a value of $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Results

After mixing the solutions of lidocaine and buprenorphine in the same syringe, no changes were observed to indicate an incompatibility (precipitation reaction). Dogs were pre-anesthetized with acepromazine 0.5 mg / kc. Epidural puncture was more difficult to perform in 2 of the 15 dogs, which were more resistant to the pre-anesthetic administered (20 minutes before restraint) and resisted manual restraint.

The anesthetic indices of epidural anesthesia performed with lidocaine, buprenorphine and the lidocaine - buprenorphine mixture are presented in table 1.

The decubitus time with buprenorphine and the lidocaine-buprenorphine mixture was longer than with lidocaine. Although there were no significant differences in the onset of analgesia with the three anesthetic protocols, the longest duration of analgesia was recorded with the lidocaine-buprenorphine mixture, the shortest in lidocaine and the medium in buprenorphine.

The averages of heart rate, mean blood pressure, respiratory rate and rectal temperature for each of the three treatment groups are shown in Tables 2, 3, 4 and 5.

There were no significant changes in the measured physiological variables.

Discussions

The administration of anesthetic agents in the epidural space is influenced by numerous factors that must be controlled, especially in this

study (age, obesity, etc.) (*Garcia-Pereira F., 2018; Smith L.J., Yu J.K., 2001*).

In clinical practice, dogs should normally be sedated (which we did using a neuroleptic phenothiazine - acepromazine 0.5 mg / kc) to facilitate epidural puncture *(Caniglia A.M. et al., 2012; Bauer M.C., 2014)*. The use of stronger preanesthetic (e.g. thiopental, xylazine, etc.) was deliberately omitted in this study to avoid the influence of these agents on physiological variables.

Epidural blockage could not be performed in two dogs due to the dislocation of the needle from the epidural space due to the agitation of the dog, which did not calm down properly. In this study it was shown that the solutions of lidocaine and buprenorphine in the mixture are miscible, thus indicating the existence of a pharmaceutical compatibility.

Epidural administration of lidocaine had the fastest lateral decubitus installation time of 1.7 ± 0.3. This is related to the excellent diffusion property and penetrability of this anesthetic agent under study (*Campoy L. 2004; Hall L.W., Clarke, K.W., 1991; Stein C. et al., 2001*).

The type and volume of local anesthetic chosen depends on the desired result. Lidocaine (2%) administered at 1 ml/6 kg completely anesthetizes the pelvic limbs and posterior abdomen, caudal to L1, within 10 to 15 minutes and lasts 60 to 120 minutes. With a comparable volume of 0.5% to 0.75% bupivacaine, the onset is 20 to 30 minutes with a duration of four to six hours. Volumes of 1 ml/7.5 kg are adequate for pelvic, perineal, and hind limb procedures (Hansen B.D., 2001).

The onset of analgesia, under the three anesthetic techniques, was not significantly different, the total duration of analgesia was longer in the case of the lidocaine-buprenorphine mixture (137.6 ± 32.9). This suggests that lidocaine and buprenorphine acted synergistically.

All parenteral formulations of buprenorphine are preservative-free and safe for epidural use (*Valverde A., 2008*). A prolonged duration of analgesia allows the performance of major diagnostic procedures, surgical and obstetric procedures, using a single anesthetic dose. The recovery time (sternal decubitus period or immediate recovery) was recorded as the longest (184.0 ± 1.5) in the case of buprenorphine epidural anesthesia, making this anesthetic unsuitable for use in situations where wants a speedy recovery.

It should be noted that the epidural administration of lidocaine, buprenorphine, lidocaine-buprenorphine mixture in dogs does not produce significant changes in heart rate, mean blood pressure, respiratory rate and body temperature. This is in line with previous reports (*Hansen B.D., 2001*) on physiological indices in buprenorphine epidural blockages in dogs.

This apparent physiological stability tells us the existence of a compensatory homeostatic mechanism in non-pre-anesthetized or slightly pre-anesthetized dogs (in our case), healthy or under the influence of other factors.

CONCLUSIONS

1. Buprenorphine may offer certain benefits for epidural use, such as a lower potential for abuse and, in some clinics, lower costs and less drug waste.

2. Epidural administration of the combination lidocaine - buprenorphine in dogs causes a strong analgesia, important for animals likely to show central hypersensitivity, a source of hyperalgesic responses and when postoperative analgesic treatment cannot neutralize the pain alone.

3. It reduces by almost 50% the amount of anesthetic agent, being characterized, in fact, by a potentiating synergistic effect.

4. This combination also causes a long-lasting analgesia of about 2 hours and excellent muscle relaxation.

5. In addition to the intra- and postoperative antinociceptive efficacy, it is observed that there were no significant respiratory and cardiac side effects and no changes in body temperature.

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Table 1.

Mean values (± SD) of the anesthetic indices (min.) Of lidocaine, buprenorphine and the combination lidocaine - buprenorphine in dogs

Anesthetic indexes	Lidocaine (a)	Buprenorphine (b)	Combination lidocaine - buprenorphine (c)
Decubitus time	1,7 ± 0,3	2,8 ± 0,7^{+}	4,8 ± 1,9^{+}
Onset of analgesia	6,0 ± 0,0	6,0 ± 1,0	6,2 ± 1,5
Duration of analgesia	83,0 ± 9,3	108,0 ± 41,6^{+}	137,6 ± 32,9^{+}
Recovery time	48,9 ± 4,0	184,0 ± 1,5	51,8 ± 12,9

Data are presented as M ± DS, + = significant differences ($p < 0.05$)

Table 2

Mean heart rate (± SD) (HR; beats / minute)

Time interval (minutes)	Lidocaine (a)	Buprenorphine (b)	Combination lidocaine - buprenorphine (c)
0	101,4 ± 5,4	116,3 ± 14,8	139,8 ± 9,8
15	86,2 ± 6,0	97,0 ± 9,9	125,0 ± 19,2
30	83,9 ± 13,6	104,0 ± 12,4	115,4 ± 12,9
45	83,7 ± 16,1	103,4 ± 14,1	117,4 ± 13,0
60	84,2 ± 13,1	102,6 ± 9,9	111,8 ± 13,6
75	90,1 ± 15,8	103,0 ± 11,4	108,0 ± 9,0

Data are presented as M ± SD

Table 3.

Mean values (± SD) of mean blood pressure (MBP; mmHg)

Time interval (minutes)	Lidocaine (a)	Buprenorphine (b)	Combination lidocaine - buprenorphine (c)
0	134,8 ± 22,3	112,0 ± 5,2	114,0 ± 10,7
15	81,3 ± 14,2	101,6 ± 7,6	111,0 ± 10,7
30	103,4 ± 13,6	104,8 ± 8,5	102,1 ± 8,1
45	112,3 ± 11,4	105,3 ± 9,1	103,1 ± 8,6
60	99,2 ± 10,3	106,6 ± 9,1	112,5 ± 16,3
75	91,4 ± 12,4	94,5 ± 6,5	99,5 ± 12,2

Data are presented as M ± SD

Table 4.

Mean values (± SD) of respiratory rate (RR; breaths / minute)

Time interval (minutes)	Lidocaine (a)	Buprenorphine (b)	Combination lidocaine - buprenorphine (c)
0	30,6 ± 4,8	22,6 ± 3,0	26,2 ± 6,8
15	19,4 ± 4,3	20,6 ± 2,4	19,4 ± 3,6
30	17,8 ± 4,3	19,8 ± 5,0	19,6 ± 2,9
45	19,1 ± 6,4	17,7 ± 2,0	19,5 ± 3,7
60	22,8 ± 9,1	17,4 ± 2,7	17,9 ± 4,0
75	24,6 ± 13,8	16,1 ± 2,9	18,2 ± 4,2

Data are presented as M ± DS

Table 5.

Mean body temperature values (± SD) (0C)

Time interval (minutes)	Lidocaine (a)	Buprenorphine (b)	Combination lidocaine - buprenorphine (c)
0	38,6 ± 0,2	39,0 ± 0,4	39,6 ± 0,3
15	39,0 ± 0,2	38,7 ± 0,3	39,4 ± 0,2
30	39,1 ± 0,2	38,8 ± 0,2	39,5 ± 0,3
45	38,7 ± 0,5	38,7 ± 0,1	39,6 ± 0,3
60	38,4 ± 0,6	38,5 ± 0,1	39,2 ± 0,3
75	38,2 ± 0,5	38,3 ± 0,1	39,0 ± 0,3

Data are presented as M ± SD