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Evaluation of transanesthetic complications comparing epidural versus analgesic continuous infusion in dogs submitted to neurosurgeries

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Abstract. Neurosurgeries have become more frequent in veterinary hospitals, however, there are some questions regarding anesthetics protocols and analgesic techniques. Thus, patient analgesia and hemodynamic stability play a key role in pre, post, and perioperative moments favoring an adequate recovery. This study aimed to evaluate the transanesthetic complications reported on anesthetic records of dogs submitted to hemilaminectomies in the university veterinary hospital of the Federal University of Santa Maria (UFSM) between January 2016 and August 2017, and compare three different analgesic protocols most commonly used in the routine for this surgery. In addition, transanesthetic parameters for each dog were equally recorded in five-minute intervals: cardiac frequency (FC), respiratory frequency (*f*) blood oxygen saturation (SpO₂), mean artery pressure (PAM), temperature and end tidal CO₂ (EtCO₂). The patients were divided into three groups: Group M: animals receiving epidural analgesia with morphine 0.1mg/kg diluted in 0.26 ml/kg of saline solution 0.9%; Group FLK: bolus of fentanyl 2 µg/kg, lidocaine 1 mg/kg, and ketamine 1 mg/kg followed by infusion of fentanyl 0.1 µg/kg/min, lidocaine 50 µg/kg/min and ketamine 10 µg/kg/min; and Group F: bolus of fentanyl 2 µg/kg followed by infusion of fentanyl 0.1 µg/kg/min. ANOVA was used to evaluate the anesthetic protocols complications, followed by Tukey's post-hoc test with a significance level of 5% (*p* < 0.05), comparing the mean of each parameter. Among the anesthetic complications that were found hypotension, bradycardia and hypercapnia were the most frequent. When 22.22% of the patients presented hypotension more evident on the first 10 minutes of anesthesia, 22.22% presented bradycardia, requiring the use of atropine (0.022 mg/kg) and 83.33% had hypercapnia on at least one of the times (EtCO₂ > 45mmHg). With this study, it was observed that the use of continuous infusions of FLK, fentanyl, and epidural analgesia with morphine, in the used doses, were effective and safe in the dogs submitted to neurosurgeries, however, it was noticed that the use of morphine caused a greater reduction in temperature during the intraoperative period.

Keywords: Analgesia, anesthesia, dogs, hemilaminectomy, neurosurgery

Evaluación de complicaciones transanestésicas comparando la epidural con la infusión analgésica continua en perros sometidos a hemilaminectomía

Resumen. La neurocirugía se ha vuelto más frecuente en los hospitales veterinarios, sin embargo, hay algunas preguntas con respecto a los protocolos anestésicos y las técnicas

analgésicas. Así, la analgesia del paciente y la estabilidad hemodinámica juegan un papel clave en el momento pre, post y perioperatorio, favoreciendo una recuperación adecuada. El objetivo de este estudio fue evaluar las complicaciones transanestésicas informadas en los registros anestésicos de perros sometidos a hemilaminectomías en el hospital veterinario universitario de la Universidad Federal de Santa María (UFSM) entre enero de 2016 y agosto de 2017, y comparar tres protocolos analgésicos diferentes más utilizados en la rutina para esta cirugía. Además, los parámetros transanestésicos para cada perro se registraron por igual en intervalos de cinco minutos: frecuencia cardíaca (FC), frecuencia respiratoria (f) saturación de oxígeno en la sangre (SpO_2), presión arterial media (PAM), temperatura y CO_2 mareomotriz ($EtCO_2$). Los pacientes se dividieron en tres grupos: Grupo M: animales que recibieron analgesia epidural con morfina 0,1 mg / kg diluido en 0,26 ml / kg de solución salina al 0,9%; Grupo FLK: bolo de fentanilo 2 μ g/kg, lidocaína 1 mg/kg y ketamina 1 mg/kg seguido de infusión de fentanilo 0,1 μ g/kg/min, lidocaína 50 μ g/kg/min y ketamina 10 μ g/kg/min; y Grupo F: bolo de fentanilo 2 μ g/kg seguido de infusión de fentanilo 0,1 μ g/kg/min. Se utilizó ANOVA para evaluar las complicaciones de los protocolos anestésicos, seguido de la prueba post-hoc de Tukey con un nivel de significación del 5% ($p < 0,05$), comparando la media de cada parámetro. Entre las complicaciones anestésicas que se encontraron, hipotensión, bradicardia e hipercapnia fueron las más frecuentes. Cuando el 22,22% de los pacientes presentaron hipotensión más evidente en los primeros 10 minutos de anestesia, el 22,22% presentó bradicardia, que requirió el uso de atropina (0,022 mg/kg) y el 83,33% tenía hipercapnia en al menos una de las veces ($EtCO_2 > 45$ mmHg). Con este estudio, se observó que el uso de infusiones continuas de FLK, fentanilo y analgesia epidural con morfina, en las dosis utilizadas fueron efectivas y seguras en los perros sometidos a neurocirugía, sin embargo se notó que el uso de morfina causó una mayor reducción en temperatura durante el período intraoperatorio.

Palabras clave: Analgesia, anestesia, perros, hemilaminectomía, neurocirugía

Introduction

Neurosurgeries are becoming increasingly constant on veterinarian hospitals routine, thus knowledge of adequate anesthetic protocols for these procedures are required. General anesthesia is essential for a surgical procedure on patients, furthermore, trans and postoperative analgesia, and maintenance of stable anesthesia is very important for animal welfare, in order to avoid morbidity and mortality during surgery (Godoi et al., 2009).

Patients with neurologic abnormalities have a need for greater anesthetic control, therefore neurologic function must be preserved at its maximum, to prevent hypoxia, hypercapnia, respiratory and cardiovascular instability (Cornick, 1992). During anesthetic procedures, it has been used multimodal analgesia, which means a drug association with distinct analgesic properties in order to block the pain from different pharmacodynamic mechanisms (Muir III et al., 2003).

This study aimed to evaluate the transanesthetic complications reported on anesthetic records of dogs submitted to hemilaminectomies in the university veterinary hospital of the Federal University of Santa Maria (UFSM) and compare three different analgesic protocols most commonly used in the routine for this surgery. In addition, the retrospective evaluation of the significance of variability from the following parameters: cardiac frequency (FC), respiratory frequency (f) blood oxygen saturation (SpO_2), mean artery pressure (PAM), temperature and end tidal CO_2 ($EtCO_2$). Then compare the same parameters amongst dogs that were submitted to hemilaminectomy, and anesthetized with morphine epidurally administered, with continuous infusion of fentanyl or association of fentanyl, lidocaine, and ketamine (FLK).

Materials and methods

Data collection was performed by analyzing medical records on the Service of Veterinary and Statistic File (SAVE) from University Veterinary Hospital located on the Federal University of Santa Maria (HVU-UFSM), between January 2016 and August 2017. A total of 67 medical records of patients manifested neurologic signs of spinal cord compression. It was selected only the medical records filled

with heart rate (HR), respiratory frequency (f), blood oxygen saturation (SpO₂), mean arterial pressure (MAP), temperature, and end-tidal CO₂ (EtCO₂). Furthermore, only medical records from patients anesthetized with the same induction protocol: propofol (Propovan®) 4 mg/kg IV plus diazepam (Diazepam®) 0.5 mg/kg IV, without pre-anesthetic medication and that were maintained in general anesthesia with isoflurane (Isoforine®) at 1.5% in spontaneous ventilation. Every patient received as support therapy dipyrone 25 mg/kg (Febrax®), cefalotine 30 mg/kg (Cefalotina Sódica®) and transoperative fluid therapy with Ringer Lactate (Ringer Com Lactato®) at a rate of 5 mL/kg/h.

Group division

Patients were divided in three groups: Group M – animals receiving epidural analgesia with morphine (Dimorf®) 0.1 mg/kg diluted in 0.26 mL/kg of saline solution 0.9%; Group FLK - fentanyl (Fentanest®) 2 µg/kg bolus, lidocaine 1 mg/kg (Cloridrato de Lidocaína 2%®) and ketamine 1 mg/kg (Cetamin®) followed by continuous infusion of fentanyl 0.1 µg/kg/min, lidocaine 50 µg/kg/min and de ketamine 10 µg/kg/min; and Group F: fentanyl bolus de 2 µg/kg followed by continuous infusion of fentanyl 0.1 µg/kg/min.

Data analysis

Anesthetic protocols were analyzed by ANOVA, followed by Tukey's post-hoc test comparing the mean of each variable (HR, f, SpO₂, EtCO₂, temperature, MAP) from animals anesthetized on Groups M, FLK, and F throughout anesthesia (5-minutes interval). T0 was considered the time in which the patient was induced and a P-value of <0,05 was considered statistically significant for all comparisons made.

Results

It was analyzed a total of 67 medical records of dogs submitted to hemilaminectomy, but only 34 were filled, and 18 fit the protocols to be evaluated in this study.

Between the dogs included in this study, 61% (11/18) were male, and 39% (7/18) females, age from animals varied from 1 to 15 years (7.5 years mean), and weight from 6.4 kg to 37.8 kg (21.7 kg mean). For the breeds in this study: (8) cross breeds, Dachshund (3), Basset Hound (2), English Bulldog (2), Beagle (1), Scottish Terrier (1), and Rottweiler (1).

The time in which animals remained anesthetized varied from 75 to 150 minutes (115 minutes mean). Since shorter anesthesia was 75 minutes, the variants of all patients were compared only until this time. Among exhibited anesthetic complications hypotension, bradycardia and hypercapnia were more frequent (Table 1). The mean temperature of animals from T0 to T75 was 37.5 °C. Whereas animals from Group M had a mean temperature of 36.4 °C, the Group FLK had 36.0 °C and Group F had 37.7 °C.

Table 1. Age, weight, sex, and anesthetic complications of each group of individuals submitted to thoracolumbar hemilaminectomy from January 2016 to October 2017.

Groups	M	FLK	F
Age Average, years	7.1	11.6	8
Weight Average, kg	10.5	14.1	14
N° of males	3	5	3
N° of females	3	1	3
Hypercapnia	6	5	4
Hypotension	-	3	1
Bradycardia	1	-	3
Analgesic Rescue	1	-	-

Group M: animals receiving epidural analgesia with morphine 0.1mg/kg diluted in 0.26 ml/kg of saline solution 0.9%; Group FLK: bolus of fentanyl 2 µg/kg, lidocaine 1 mg/kg and ketamine 1 mg/kg followed by infusion of fentanyl 0.1 µg/kg/min, lidocaine 50 µg/kg/min and ketamine 10 µg/kg/min; and Group F: bolus of fentanyl 2 µg/kg followed by infusion of fentanyl 0.1 µg/kg/min.

Regarding anesthetic complications 22.22% (4/18) of patients showed hypotension (MAP < 60 mmHg) being more evident on first 10 minutes of anesthesia, 22.22% (4/18) exhibited bradycardia (HR < 20% normal baseline) demanding to use atropine (0.022 mg/kg), and 83.33% (15/18) demonstrated hypercapnia at least once (EtCO₂ > 45 mmHg), in most animals after 60 minutes of anesthesia. It was required to use vasopressor in 16.66% (3/18) of animals, two with dobutamine 5 µg/kg/min (Cloridrato de Dobutamina®) 5, one with dopamine 5 µg/kg/min (Cloridrato de Dopamina®) 5, and one patient needed analgesic rescue with fentanyl 2.5 µg/kg at the beginning of surgery.

Temperature presented a significant difference when compared to M to FLK and M to F, thus patients from Group M had greater body temperature reduction, even though they showed a higher mean temperature. The remaining variants displayed no difference in none of the three protocols.

Discussion

It is important to give special attention to pain control and management to ensure animal welfare and provide better recovery conditions for patients that were submitted to surgery or traumatized. Many strategies can be employed for pain treatment, therefore the professional must choose previously what drugs available will be used, always considering the patient, surgical procedure, and level of pain to which animal will be exposed (Fantoni & Cortopassi, 2009).

Contrasting with the results found by Godoi et al. (2009) where 26 from 54 animals submitted to neurosurgery were females and the predominant breed was Dachshund (22 dogs); this study showed a higher prevalence of males and crossbreeds. According to the same author, mean time of surgery on patients that were submitted to hemilaminectomy was 2 hours and 34 minutes (Godoi et al., 2009) which is way above mean time of anesthesia (1 hour and 55 minutes) for the same surgical procedure on the patients from this study.

Morphine is a prototype opiate analgesic that acts on μ , κ , and δ receptors. It is relatively hydrophilic and very useful for analgesia of dogs, cats, equines, and rodents. Regarding the adverse effects, there is a potential risk of histamine release and vomiting (Lamont & Mathews, 2013). Epidural administration of morphine has been employed with good results for pain management, like this study, without observation of adverse effects mentioned above. There are differences in opioids pharmacodynamics for CNS receptors among animal species, but in general, epidural analgesia is mediated by activation of μ -1, μ -2, κ and δ receptors (Valadão et al., 2002).

Epidural access in small animals is performed usually on the lumbosacral site (L7-S1) (Godoi et al., 2009), hence this region is chosen to administrate analgesia with morphine on animals from Group M. However, it is possible to access the epidural site at any intervertebral space from the lumbar spine (Klaumann & Otero, 2013). Regarding dogs and cats, it is preconized a total volume of epidural injection of 0.2 mL/kg but does not exceed 6 mL for animals weighing more than 30 kg. It was used distinct volumes from different drugs where the amount administered was between 0.13 and 0.36 mL/kg without the occurrence of adverse effects (Valverde, 2008).

The use of different drugs in continuous infusion techniques produces several benefits on balanced anesthesia, such as a minor requirement from the inhaled anesthetic and better pain control. The most commonly used in these protocols are local anesthetics, dissociative drugs, and opioids, which can be administered isolated or in association (Cerejo et al., 2013). Moreover, these analgesic agents act on different stages of a painful process, such as transduction, transmission, and integration, blocking nociception in different points, therefore this pharmacological synergy favors drug biotransformation and also allows its dose reduction (Muir III et al., 2003).

Fentanyl is a synthetic opioid agonist of μ receptors. When compared to morphine, fentanyl is 100 times stronger and more lipophilic, this drug has a fast onset and a short-term action. The administration of IV bolus of fentanyl (1 - 5 µg/kg) followed by continuous infusion (1 - 5 µg/kg/hour) provides suitable sedation and post-surgical analgesia (Gremião et al., 2018).

Ketamine has been often administered as part of a balanced anesthetic protocol due to its analgesic features, mainly when is used at subanesthetic dosages. This drug also reduces anesthetic requirements, maintaining hemodynamics parameters stable, and its analgesic property is attributed to the antagonistic

effect on N-methyl-D-aspartate (NMDA) spinal cord receptors. Besides, ketamine also acts on opioid and muscarinic receptors (Carregaro et al., 2010).

Lidocaine has a local analgesic effect when used on continuous infusions and its use has been largely discussed in past years. It acts as preventing sympathetic responses that occur by surgical stimulus and reduces intraoperative use of opioids without promoting significant hemodynamic instabilities. The use of lidocaine on continuous infusion at 50 µg/kg/min reduced 18.7% of isoflurane and the absence of cardiovascular side effects on healthy dogs (Carregaro et al., 2010).

Hypotension and hypoventilation were complications related by Cerejo et al. (2013), which hypotensive episodes responded to vasopressor drugs or fluid therapy bolus, similarly to our study. According to the same author, there was an increase in end-tidal CO₂ (> 50 mmHg) on 7.5% of evaluated dogs, differing from this paper with higher rates of animals with hypercapnia and absence of mechanic ventilation.

Apnea and cardiac arrhythmia (atrioventricular block and ventricular tachycardia) were also related in animals receiving FLK infusion (Cerejo et al., 2013), however, in this study, no animals exhibited these complications. Compared with other studies, where 25% of animals anesthetized with isoflurane for neurosurgeries showed bradycardia (Godoi et al., 2009), our study showed no difference in our evaluations (22.22%).

Heat loss from animals may occur by radiation, convection, conduction, skin evaporation, expired air, animal wastes (urine and feces), and CO₂ release, thus, the use of surgical solutions, trichotomy, cold environment, and metabolism depression by anesthesia are important factors of body temperature decrease (Yazbek, 2010). The hypothalamus thermoregulator system is also affected by opioid administration (Biazzotto et al., 2006). Animals from the morphine group received antisepsis with alcohol-iodine-alcohol for peridural puncture and also had surgical antisepsis with chlorhexidine digluconate solution 1%, followed by chlorhexidine digluconate alcoholic solution 0.5 %, being exposed to subsequent processes of heat loss by evaporation, therefore this is a hypothesis to explain a significant temperature reduction.

Conclusions

In this study we observed that continuous infusion of FLK, fentanyl, and epidural analgesia with morphine were safe and effective on dogs submitted to neurosurgeries, however, it was demonstrated that the use of morphine caused a significant temperature reduction on transoperative, being necessary caution to avoid hypothermia. Also, hypercapnia results were significant, because it was more frequent than related from other authors, emphasizing the importance of mechanic ventilation for neurosurgeries. Thus, we conclude that more studies evaluating other parameters, such as cardiac output, central venous pressure, and hemogasometry are required.

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