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Behavior of the Bispectral Index (BIS) and Electromyography (EMG) in Bitches Undergoing Ovariohysterectomy

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ABSTRACT

***Background*:** The bispectral index (BIS) is a method used to monitor patients during surgical procedures. However, studies on the use of BIS in bitches anesthetized with different protocols and undergoing ovariohysterectomy are scarce in the literature. This study aimed to assess the behavior of BIS and electromyography (EMG) in bitches anesthetized with ketamine and midazolam in combination with xylazine, medetomidine, or dexmedetomidine.

***Materials, Methods & Results*:** Thirty bitches anesthetized with ketamine and midazolam were divided into 3 groups of 10 animals each: dexmedetomidine (20 µg/kg/h), medetomidine (30 µg/kg/h), and xylazine (1000 µg/kg/h). All animals underwent an 8-h fasting period for food and a 2-h water restriction before surgery. A trichotomy was performed in the frontal and temporal regions to allow for the placement of BIS monitor sensors, as well as on the thoracic limbs for venous catheter insertion. The animals were maintained under spontaneous ventilation, receiving an inspired oxygen fraction of 100% at a continuous gas flow rate of 20 mL/kg/min. Vital parameters were monitored using a multiparameter monitor. BIS and EMG values were recorded using a BIS monitor at the following time points: before pre-anesthetic medication (control), 15 min after pre-anesthetic medication, 10 min after anesthetic induction and orotracheal intubation, at the end of the ovariohysterectomy, and 30 min after the beginning of the surgical procedure. Postoperatively, all animals received meloxicam (0.2 mg/kg) subcutaneously for analgesia. Upon regaining quadrupedal posture, they were discharged to their owners with prescriptions for meloxicam (0.2 mg/kg) every 24 h for 3 days and dipyrone (20 mg/kg) every 8 h for 5 days, both administered orally. A one-way analysis of variance (ANOVA) was performed to compare the means of each variable at different time points, followed by a post-hoc Tukey test. A significance level of 5% was adopted. A significant reduction in BIS was observed after pre-anesthetic medication only in the dexmedetomidine group ($P < 0.05$). After anesthetic induction, BIS values progressively decreased in all groups, with the dexmedetomidine group showing significantly lower values compared to the medetomidine and xylazine groups. EMG values significantly decreased in all groups throughout the study period.

***Discussion*:** The study's hypothesis was partially confirmed, as only the dexmedetomidine group showed significantly lower BIS and EMG values compared to the other groups at 15 min after pre-anesthetic medication and 10 min after anesthetic induction and orotracheal intubation. The lower BIS and EMG values observed in the dexmedetomidine group at 15 min after pre-anesthetic medication and 10 min after anesthetic induction and orotracheal intubation align with findings from previous studies using dexmedetomidine via continuous infusion or epidural administration. However, this reduction contradicts findings from other studies suggesting that BIS is not applicable in patients receiving ketamine. Studies have shown that dogs treated with medetomidine/isoflurane exhibit a marked BIS reduction compared to those receiving isoflurane alone. Similarly, in rats, EMG values significantly decreased following drug infusion. However, the results of this study suggest a disproportionate reduction between BIS and EMG values. Dexmedetomidine provided adequate anesthesia for ovariohysterectomy, as evidenced by the significant reductions in BIS and EMG values.

Keywords: alpha-2 agonist, dogs, continuous infusion, TIVA.

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INTRODUCTION

The monitoring of surgical patients ranges from sedation to anesthesia requiring prolonged and deeper anesthetic planes, with the bispectral index (BIS) standing out due to its reliability in performing this monitoring [9,16]. BIS values are generated from the patient's electroencephalogram (EEG) signals, which are immediately converted into digital signals, filtered to eliminate artifacts, and divided into two-second epochs [13]. It is obtained through Fourier transformation and bispectral analysis, resulting in a multivariate statistical analysis that incorporates spectral power, bispectral, and burst suppression parameters correlating with hypnotic activity [5,13].

Monitoring hypnotic depth using BIS has been the subject of study in various research fields and is commonly employed in the anesthetic routines of most human hospitals [1,7,11]. However, there remains a limited amount of research in Veterinary Medicine.

Currently, the combination of different pharmacological agents, especially those with a higher specificity for α2-agonist receptors (e.g., dexmedetomidine, medetomidine, and xylazine), is being explored [15-19]. Nevertheless, medetomidine affects electroencephalography at both low and high frequencies, and its administration in continuous infusion warrants further investigation [8].

This study aims to evaluate the behavior of the bispectral index (BIS) and electromyography (EMG) in bitches anesthetized with ketamine and midazolam, in combination with xylazine, medetomidine, or dexmedetomidine, and undergoing ovariohysterectomy.

MATERIALS AND METHODS

Inclusion and exclusion criteria

Bitches with no abnormalities in their physical examination, hematological profile, or serum biochemical analysis (alanine aminotransferase and creatinine), as well as normal electrocardiogram and echocardiogram results, were included in the study.

Animals presenting any alterations in the aforementioned examinations or those that had received any medication within 30 days prior to the study were excluded.

Experimental procedure

Thirty healthy adult, mixed-breed, non-spayed, medium-sized female dogs were used and randomly divided into 3 groups of 10 animals each, according to the drug administered in combination with ketamine hydrochloride and midazolam: Group 1 (G1): Dexmedetomidine, Group 2 (G2): Medetomidine, and Group 3 (G3): Xylazine.

All animals underwent an 8-h pre-surgical fasting period for food and a 2-h water restriction. A trichotomy was performed in the frontal and temporal regions for the placement of bispectral index (BIS) monitor sensors, as well as on the thoracic limbs for venous catheter insertion.

All animals received pre-treatment with levomepromazine[1] [Levozine® - 1.0 mg/kg] and morphine sulfate[1] [(Dimorf® - 0.3 mg/kg], both administered intravenously (IV). Fifteen min later, anesthetic induction was performed with ketamine hydrochloride[2] [Quetamina® - 2.0 mg/kg, IV] and midazolam maleate[1] [Dormire® - 0.2 mg/kg, IV]. This was followed by continuous IV administration of hydrochloride[2] [Quetamina® - 20 mg/kg/h] and midazolam maleate1 [Dormire® - 0.4 mg/kg/h] in combination with chloridrate of dexmedetomidine[3] [Dexdomitor®- G1 - 20 µg/kg/h], medetomidine[3] [Medetomidina® - G2 - 30 µg/kg/h], and xylazine[4] [Xilazin® - G3 - 1000 µg/kg/h). This continuous infusion was maintained for 30 min.

The animals were maintained under spontaneous ventilation, receiving an inspired oxygen fraction of 100% at a continuous gas flow of 20 mL/kg/min. Vital parameters were continuously monitored using a multiparameter monitor.

All ovariohysterectomy procedures were performed at 8:00 AM by the same surgeon. A 4 cm retro-umbilical incision was made, and hemostasis of the ovarian vein and artery was achieved using Kelly hemostatic forceps, with vascular ligation performed using 2-0 polyglactin 910 sutures.

BIS and electromyographic (EMG) evaluations were recorded using a BIS Aspect A 2000Xp[5] monitor at the following time points: prior to pre-anesthetic medication (control) (TP_0), 15 min after pre-anesthetic medication (TP_1), 10 min after anesthetic induction and orotracheal intubation (TP_2), at the end of the ovariohysterectomy (TP_3), and 30 min after the beginning of the surgical procedure (TP_4).

Following surgery, all animals received postoperative analgesia with meloxicam [0.2 mg/kg, subcutaneously]. Once they regained quadrupedal posture, they were discharged to their owners with prescriptions

of meloxicam[2] [Meloxinew® - 0.2 mg/kg, SID, orally] for 3 days and dipyrone[6] [Dipirona Monoidratada 500 mg® - 20 mg/kg, TID, orally] for 5 days.

Statistical analysis

A variance analysis (ANOVA) was performed to compare the averages of each variable studied in the different time points, followed by *post-hoc* analysis using the Tukey test. A 5% significance level was adopted.

RESULTS

No complications were observed during the surgical and/or anesthetic procedures throughout the study. The animals presented a body mass between 15 and 25 kg (average ± mean deviation: 20 ± 5 kg) and age from 12 to 36 months (24 ± 8 months).

A significant decrease ($P < 0.05$) in BIS occurred after the administration of the pre-anesthetic medication solely on group G1 (dexmedetomidine) [Table 1]. The G1 group showed significantly lower values ($P < 0.05$) when compared to the other groups, at TP1 and TP2 [Table 1].

Regarding the electromyography, significantly lower values ($P < 0.05$) were identified in group G1 (dexmedetomidine), 15 min after the pre-anesthetic medication (TP1) [Table 2].

Table 1. Bispectral index (BIS) of the bitches anesthetized with the combination of ketamine hydrochloride and midazolam, and subjected to dexmedetomidine (G1), medetomidine (G2), and xylazine (G3) at the time points (TP_0 - $TP_{4)}$.

Groups	TP_0	TP_1	TP_2	TP_3	TP_4
G1	98.2 ± 0.42^{Aa}	87.1 ± 9.06^{Aa}	74.2 ± 6.65^{Aa}	66.1 ± 9.22^{Aa}	63.0 ± 7.44^{Aa}
G2	98.8 ± 0.42^{Aa}	98.3 ± 0.48^{Ba}	81.7 ± 4.50^{Ba}	72.5 ± 5.40^{Aa}	65.2 ± 8.20^{Aa}
G3	98.5 ± 0.71^{Aa}	98.3 ± 0.48^{Ba}	80.9 ± 6.94^{Ba}	71.9 ± 7.94^{Aa}	68.1 ± 7.03^{Aa}

Different uppercase letters within the columns indicate significant differences, through the Tukey test. Time points: prior to the pre-anesthetic medication (TP_0), 15 min after pre-anesthetic medication (TP_1), 10 min after anesthetic induction and orotracheal intubation (TP_2), at the end of the ovariohysterectomy (TP_3), and 30 min after the beginning of the surgical procedure (TP_4).

Table 2. Electromyography (EMG) of bitches anesthetized with the combination of ketamine hydrochloride and midazolam, and subjected to dexmedetomidine (G1), medetomidine (G2), and xylazine (G3) at the time points (TP_0 - TP_4).

Groups	TP_0	TP_1	TP_2	TP_3	TP_4
G1	99.9 ± 0.32^{Aa}	69.2 ± 10.26^{Aa}	49.4 ± 11.71^{Aa}	34.0 ± 7.20^{Aa}	27.7 ± 2.00^{Aa}
G2	99.9 ± 0.32^{Aa}	$86{,}4 \pm 3{,}53^{Ba}$	44.3 ± 14.48^{Aa}	31.5 ± 8.89^{Aa}	25.1 ± 6.49^{Aa}
G3	100 ± 0.00^{Aa}	85.0 ± 6.48^{Ba}	43.1 ± 9.97^{Aa}	31.0 ± 8.68^{Aa}	25.0 ± 6.94^{Aa}

Different uppercase letters within the columns indicate significant differences, through the Tukey test. Time points: prior to the pre-anesthetic medication (TP_0), 15 min after pre-anesthetic medication (TP_1), 10 min after anesthetic induction and orotracheal intubation (TP_2), at the end of the ovariohysterectomy (TP_3), and 30 min after the beginning of the surgical procedure (TP_4).

DISCUSSION

The current study aimed to evaluate the behavior of the bispectral index (BIS) and electromyography (EMG) in bitches anesthetized with ketamine and midazolam combined with dexmedetomidine, medetomidine, or xylazine and subjected to the ovariohysterectomy surgical procedure, given that studies on BIS in bitches anesthetized with different protocols are scarce in the literature. The findings of this study may provide a foundation for using BIS as a method to monitor hypnotic depth during anesthetic procedures in dogs. Only the dexmedetomidine group presented significantly lower values of BIS and EMG when compared to the other groups at 15 min after pre-anesthetic medication and 10 min post anesthetic induction and orotracheal intubation time points. Such BIS reduction was previously observed in similar research [17]. The administration of dexmedetomidine on a continuous infusion [9], or epidurally [3], promoted BIS reduction.

The use of BIS for anesthetic monitoring in continuous IV infusion with the combinations and doses proposed in the current study according to the literature [17]. A significant reduction in BIS and EMG in the dexmedetomidine-treated group contradicting findings from different studies [10,12]. These authors considered BIS not applicable in patients treated with ketamine. No values below 82 were observed in animals treated with levomepromazine/midazolam/ketamine/xylazine [16]. Dogs treated with medetomidine/isoflurane presented a marked reduction in BIS when compared to dogs treated with isoflurane alone, corroborating the findings of [6].

Similar to what was observed in rats [2,14], EMG significantly decreased after the start of drug infusion. However, the results suggested a disproportion between the BIS and EMG reductions, aligning with the literature [3,17]. Dexmedetomidine was found to provide of sedation comparable to that of midazolam, but without the same degree of amnesia [4].

CONCLUSION

Dexmedetomidine provided adequate anesthesia for performing ovariohysterectomy in medium-sized, mixed-breed bitches as evidenced by the significant reduction of Bis and EMG values.

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Ethical approval. The study was approved by the Ethics Committee in the Use of Animals of the Federal University of RO (UNIR) (Protocol No 004/2014). The animals' owners signed informed consent form agreeing to the inclusion of the animals in the study.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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