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Sedative Effects of Medetomidine and Dexmedetomidine in Cats - Evaluation with Bispectral Index Monitoring (BIS)

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ABSTRACT

***Background*:** Sedation is a state of sleepiness and relaxation that results from the depression of the central nervous system. The depth of sedation can be assessed by hemodynamic responses and neurological signs, such as the palpebral reflex, startle response, nystagmus, and response to stimuli. Currently, the Bispectral Index (BIS) is considered the most accurate monitor for assessing brain function during anesthesia and sedation. BIS values for deep sedation between 60-70, and mild to moderate sedation between 70-90. Values above 90 indicate that the patient is awake. This study aims to compare the sedative effects of medetomidine and dexmedetomidine by evaluating the physical examination findings that indicate the depth of sedation, alongside the BIS monitoring, which is an objective monitoring method.

***Materials, Methods & Results*:** In this study, 100 cats brought to the Istanbul University-Cerrahpasa Faculty of Veterinary Science, Department of Surgery, Otorhinolaryngology (ENT) Clinic between 2018 and 2022, and indicated for Ventral Bulla Ostectomy (VBO) following examinations, were evaluated for BIS findings and physical examination results after sedation administration. Patients with 1st and 2nd degree anesthesia risk according to the ASA, based on physical, laboratory, and radiological examinations, were included in the study. The 100 patients were randomly divided into 2 groups of 50 each. Following the pre-anesthetic examination, butorphanol (0.4 mg/kg) was administered subcutaneously in both groups preemptively. After 10 min of butorphanol administration, intravenous access through the vena cephalica or vena saphena was obtained using a 22 or 24 gauge angiocath. Medetomidine HCl IV was used for sedation in the 1st group, while Dexmedetomidine HCl (20 µg/kg) IV was used in the 2nd group. After the patients were sedated and complete relaxation was achieved, the self-adhesive sensors of the BIS probe were placed on the frontal region. Posture, jaw tone, palpebral reflex, corneal reflex, pupil size, and limb withdrawal reflex (LWR) were evaluated and recorded before sedation (T0) and at the 5 min following sedation (T1).

***Discussion*:** Alpha-2 adrenoceptor agonists can affect both postural and smooth muscles. Relaxation of postural muscles may manifest as recumbency or ataxia. This study's findings were consistent with existing literature: all patients were in lateral recumbency after 5 min following alpha-2 administration, exhibited decreased jaw tone, and allowed their mouths to be opened easily. Moderate sedation in humans is defined as a reversible state in which response to tactile and vocal stimuli is preserved. However, when considering the BIS and LWR findings, we observed that 72% of the moderately sedated patients in the 1st group lost the LWR reflex, which evaluates the response to painful stimuli. This response to painful stimuli, which is more significant than tactile stimuli, partially contradicts the literature. In addition to considering that different sedative drugs may yield different findings, it was believed that the strong muscle relaxant and analgesic properties of medetomidine could explain the results without causing loss of consciousness. In the intergroup evaluation, the mean BIS value of the 1st group was 72.82, indicating moderate sedation. In contrast, the mean BIS value of the 2nd group was 67.12, which was classified as deep sedation. Contrary to the literature, the BIS findings between the groups showed that deeper sedation occurred in the dexmedetomidine group. Based on the BIS findings, we believe that dexmedetomidine will be more effective than medetomidine in procedures requiring procedural sedation by inducing a hypnotic state close to general anesthesia.

Keywords: sedative drugs, brain function monitor, BIS findings, LWR (limb withdrawal reflex), sedation, palpebral reflex.

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INTRODUCTION

Sedation is a state of sleepiness and relaxation accompanied by depression of the Central Nervous System [20,23,24,27,29,33,36]. According to the American Society of Anesthesiologists (ASA), sedation is classified into superficial, moderate, and deep sedation. Superficial sedation is a reversible drug-induced state in which patients respond normally to audible stimuli. Moderate sedation (conscious sedation) is a reversible state where consciousness is moderately suppressed due to drugs, but response to tactile and vocal stimuli is preserved. Airway intervention is not required, spontaneous breathing is adequate, and cardiovascular function is not affected. Deep sedation is a reversible state where consciousness is significantly suppressed due to medication, and patients do not respond easily to verbal stimuli. Intervention may be required to maintain airway patency, spontaneous respiration is usually inadequate, but cardiovascular functions are generally preserved. [4,11,32].

BIS is currently considered the most accurate brain function monitor for use in anesthesia and sedation monitoring [3,9,24]. The BIS value is calculated in real time from EEG data recorded 15-20 s before the measurement. It ranges between 0 and 100 [1-3,6,18,28]. Values between 60-70 indicate deep sedation, and 70-90 indicate mild to moderate sedation. Values above 90 indicate that the patient is awake. [18,26].

This study aims to compare the sedative effects of medetomidine and dexmedetomidine by evaluating the physical examination findings that indicate the depth of sedation, alongside the BIS monitoring, which is an objective monitoring method.

MATERIALS AND METHODS

Materials

In this study, 100 cats brought to the Istanbul University-Cerrahpasa Faculty of Veterinary Science, Department of Surgery, Otorhinolaryngology (ENT) Clinic between 2018 and 2022, and indicated for Ventral Bulla Ostectomy (VBO) based on examinations, were evaluated in terms of BIS findings and physical examination findings following sedation. The patients, aged 0-7 years, presented to the ENT clinic with complaints of ear discharge, Horner's Syndrome, head tilt, and imbalance. Following otologic examination, computed tomography of the cranium with ear, nose, and throat localization was requested for patients with suspected otitis media and inflammatory ear polyps. In cases where computed tomography revealed soft tissue or fluid contrast in the tympanic cavity and wall thickening in the tympanic bullae, a diagnosis of otitis media or inflammatory ear polyps was made, and VBO was planned for treatment.

Investigations

Laboratory investigations and radiographic examinations were performed for routine operative preparation. For this purpose, complete blood count (Erythrocyte-RBC, Hemoglobin-HGB, Hematocrit-HCT, Leukocyte-WBC, Platelet-PLT) and anesthesia protocol biochemistry parameters (Glucose-GLU, Creatinine-CREA, Blood Urea Nitrogen-BUN, BUN/CREA, Phosphate-PHOS, Calcium-CA, Total Protein-TP, Albumin-ALB, Globulin- GLOB, ALB/GLOB, Alanine aminotransferase-ALT, Aspartate aminotransferase-AST, Alkaline phosphatase-ALKP, Gamma glutamyltransferase-GGT, Total bilurubin-TBIL, Cholesterol-CHOL) were measured. Right and left laterolateral and dorsoventral thoracic radiographs were ordered for preanesthetic evaluation of the airway, pulmonary parenchyma, mediastinum and pleural cavity.

Patients assessed with 1st or 2nd-degree anesthesia risk according to ASA classification, based on physical examination, laboratory, and radiological findings, were included in the study. A total of 100 patients were randomly divided into 2 groups, each consisting of 50 patients. Following the preanesthetic examination, butorphanol[1] [Butorphanol® - 0.4 mg/kg, SC, SID] was administered according to the same protocol in both groups. Intravenous access was established through the cephalic or saphenous vein using a 22 or 24 gauge angiocath[2] [Intraket®], approximately 10 min after butorphanol administration. Medetomidine HCl[3] [Tomidin® - 40 µg/kg, IV, SID] was administered to the 1st group, while Dexmedetomidine HCl[4] [Hipnodex® - 20 µg/kg, IV, SID] was administered to the 2nd group for sedation.

After achieving sedation and ensuring complete relaxation, the frontal region was shaved using a blade razor numbered 40 to apply the self-adhesive sensors of the BIS probe. The area was then cleaned with alcohol and dried, repeating the process twice for thoroughness. A Pediatric BIS probe was chosen due

to its suitability for cat sizes. Sensor number 1 of the Pediatric BIS probe was positioned in the middle of the frontal region, while sensor number 2 was placed to the right of sensor number 1 in a parallel orientation. The probe was then rotated, with sensor number 4 placed below sensor number 2 and sensor number 3 positioned under sensor number 1. Once the BISx[5] and monitor interface were established, a connection was established between the BISx interface and the sensor[5] [BIS Pediatric®], and subsequently with the patient via the BIS Monitor[5] [BIS Complete Monitoring System P/N 185-0151®]. BIS measurement commenced 5 min after sedation for all patients (Figure 1).

After sedation, all patients were connected to the bedside monitor[6] [Multiparameter Veterinary Monitor, GT9003E®]. Heart rate and respiratory rate were measured using clip-on ECG electrodes. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were measured noninvasively with a sphygmomanometer integrated into the same device. SpO_2 was monitored using the tongue probe of the pulse oximeter. Additionally, body temperature was continuously monitored using a rectal probe.

Before sedation (T0), posture, jaw tone, palpebral reflex, corneal reflex, corneal reflex, pupil size and limb withdrawal reflex (LWR) of all patients were evaluated and recorded. At the 5 min following sedation (T1), posture, jaw tone, palpebral reflex, corneal reflex, pupil size and limb withdrawal reflex (LWR) were re-evaluated in all patients. After the connection of BIS monitoring was established, BIS and EMG values were automatically recorded.

The data collected in this study were analyzed using the licensed SPSS 25 software package. Skewness and kurtosis coefficients were employed to assess whether the variables followed a normal distribution. Following Tabachnik and Fidell's guidelines (2013), if the skewness and kurtosis values fell within the range of -1.50 to +1.50, it was considered indicative of a normal distribution. To examine differences between groups, the independent samples *t*-test was utilized for normally distributed variables. Similarly, for comparisons within dependent groups, the dependent samples *t*-test was employed. A significance level of 0.05 was adopted for interpreting the results, indicating a significant difference for $P < 0.05$ and no significant difference for $P > 0.05$.

Figure 1. Patient connection with BIS monitor.

RESULTS

At the initial assessment (T0), all patients were standing and in the sternal position, displaying resistance to jaw tension control due to wakefulness. The corneal reflex, palpebral reflex, and limb withdrawal reflexes were preserved in all patients, and pupil size was normal. After sedation (T1), which occurred 5 min following the administration of medetomidine and dexmedetomidine, patients were observed to gradually shift from their normal posture to a lateral recumbent position. It was noted that all patients exhibited easy mouth opening, with relaxation in jaw tone. Reflexes showed a decrease compared to T0, and while pupil size generally remained normal, slight changes were observed post-sedation. At T1, the palpebral reflex was preserved in 65 patients but disappeared in 35 patients. The corneal reflex was present in 76 patients but absent in 24 patients. Pupil size remained normal in 21 patients but became mydriatic in 77 patients. In 2 patients, pupil size evaluation was hindered due to pannus. Limb withdrawal reflex was elicited in 21 patients but was absent or disappeared in 79 patients. The mean BIS value was 72.82, and the mean EMG value was 38.46% (Table 1).

In the medetomidine group, sedation exhibited a statistically significant impact on physical examination findings. The palpebral reflex showed a significant difference with $t(49) = -4.365$, $P = 0.001$, indicating a significant effect of sedation. Similarly, the corneal reflex demonstrated significance with $t(49) = -2.585$, $P = 0.013$, suggesting an effect of sedation. Pupil size exhibited a notable difference between the awake and sedated states, calculated as $t(49) = -14.000$, $P = 0.001$,

indicating a significant effect of sedation. Additionally, the limb withdrawal reflex (LWR) showed a significant difference with t (49) = -11.220, $P = 0.001$, confirming the impact of sedation as $P < 0.05$, signifying a statistically significant difference between the awake and sedated states (Table 2).

Dexmedetomidine group showed similar findings to medetomidine group. Palpebral reflex calculated as t (49) = -5.957, $P = 0.001$; corneal reflex calculated as t (49) = -5.250, $P = 0.001$; pupil size calculated as t (47) = -12.570, $P = 0.001$; and LWR calculated as t(49) = -17.350, $P = 0.001$. Pupil size and LWR showed a very strong difference between baseline and sedation results (Table 3).

In the BIS measurement at T1, the mean BIS value of the 1st group was 72.82 and the mean BIS value of the 2nd group was 67.12. There was a significant difference between the 1st and 2nd groups in terms of mean BIS values [t (98) = 2.259, $P = 0.026$]. At T1, the mean EMG value of the 1st group was 38.46 ± 4.91%; and the mean EMG value of the 2nd group was 37.22 ± 4.01%. There was no significant difference between the 1st and 2nd groups in terms of mean EMG values [t (98) = 1.383, $P = 0.171$] (Table 4).

At T1, patients with preserved palpebral reflex had a mean BIS value of 72.09, whereas those without had a mean BIS value of 66.03. A significant difference in BIS values was observed between patients with and without palpebral reflex preservation [t (98) = 2.294, $P = 0.024$]. Similarly, at T1, patients with a corneal reflex had a mean BIS value of 72.01, while those without had a mean BIS value of 63.50. There was a significant difference between the BIS values of patients with and without corneal reflex [t (98) = 2.931, $P = 0.004$]. No significant difference was observed between patients with normal pupil size and those with mydriatic pupils at T1 [t (94) = 0.484, $P = 0.631$]. Lastly, at T1, patients with preserved limb withdrawal reflex (LWR) had a mean BIS value of 75.52, whereas those with lost LWR had a mean BIS value of 68.49. A significant difference was found between the BIS values of patients with and without preserved LWR [t (98) = 2.301, $P = 0.028$] (Table 5).

Table 1. T_0-T_1 Physical examination, Distribution of BIS and EMG results.

Variable	Category	Group			
		1st Group (Medetomidine)		2nd Group (Dexmedetomidine)	
		n	%	n	%
Palpebral Reflex T_0	Present	50	50.00	50	50.00
	Absent	0	0.00	0	0.00
Palpebral Reflex T_1	Present	36	55.38	29	44.62
	Absent	14	40.00	21	60.00
Corneal Reflex T_0	Present	50	50.00	50	50.00
	Absent	0	0.00	0	0.00
Corneal Reflex T_1	Present	44	57.89	32	42.11
	Absent	6	25.00	18	75.00
Pupil Size T_0	Normal	50	50.00	50	50.00
	Mydriatic	0	0.00	0	0.00
Pupil Size T_1	Normal	10	47.62	11	52.38
	Mydriatic	40	51.95	37	48.05
LWR T_0	Present	50	50.00	50	50.00
	Absent	0	0.00	0	0.00
LWR T_1	Present	14	66.67	7	33.33
	Absent	36	45.57	43	54.43
Variable		Mean ± SD	Min - Max.	Mean ± SD	Min - Max.
BIS		72.82 ± 12.91	46-97	67.12 ± 12.31	32-94
EMG		38.46 ± 4.91	29-51	37.22 ± 4.01	29-48

Table 2. T_0-T_1 comparison of physical examination findings of the 1st group.

Variable	Mean	N	SD	*t*	*P*
Palpebral Reflex T_0	1.00	50	0.00	-4.365	0.001*
Palpebral Reflex T_1	1.28	50	0.45		
Corneal Reflex T_0	1.00	50	0.00	-2.585	0.013*
Corneal Reflex T_1	1.12	50	0.33		
Pupil Size T_0	1.00	50	0.00	-14.000	0.001*
Pupil Size T_1	1.80	50	0.40		
LWR T_0	1.00	50	0.00	-11.220	0.001*
LWR T_1	1.72	50	0.45		

*$P < 0.05$. *t:* dependent samples *t*-test.

Table 3. T_0-T_1 comparison of physical examination findings of the 2nd group.

Variable	Mean	N	SD	*t*	*P*
Palpebral Reflex T_0	1.00	50	0.00	-5.957	0.001*
Palpebral Reflex T_1	1.42	50	0.50		
Corneal Reflex T_0	1.00	50	0.00	-5.250	0.001*
Corneal Reflex T_1	1.36	50	0.48		
Pupil Size T_0	1.00	48	0.00	-12.570	0.001*
Pupil Size T_1	1.77	48	0.42		
LWR T_0	1.00	50	0.00	-17.350	0.001*
LWR T_1	1.86	50	0.35		

*$P < 0.05$. *t:* dependent samples *t*-test.

Table 4. Comparison of BIS and EMG at T_1 according to groups.

Variable	Category	Group		*t* test	
		Mean	SD	*t*	*P*
BİS T_1	Medetomidine	72.82	12.91	2.259	0.026*
	Dexmedetomidine	67.12	12.31		
EMG T_1	Medetomidine	38.46	4.91	1.383	0.171
	Dexmedetomidine	37.22	4.01		

*$P < 0.05$. *t:* independent samples *t*-test.

Table 5. Comparison of BIS and physical examination findings at T_1.

Variable	Category	BIS T_1		*t* test	
		Mean	SD	*t*	*P*
Palpebral Reflex	Present	72.09	13.19	2.294	0.024*
	Absent	66.03	11.43		
Corneal Reflex	Present	72.01	12.91	2.931	0.004*
	Absent	63.50	10.63		
Pupil Size	Normal	71.14	12.99	0.484	0.631
	Mydriatic	69.60	12.97		
LWR	Present	75.52	12.39	2.301	0.028*
	Absent	68.49	12.67		

*$P < 0.05$. *t:* independent samples *t*-test.

DISCUSSION

Physical methods utilized for monitoring the CNS during anesthesia encompass the regulation of muscle tone, eye position, pupil size, and control of palpebral and corneal reflexes [3,9,10,14,34]. In this study, we employed these physical methods for sedation monitoring, drawing from foundational literature [3,9,10,14,34]. Additionally, the impact of the optical isomers medetomidine and dexmedetomidine on the hypnotic state was assessed through BIS monitoring.

Alpha-2 adrenoceptor agonists can influence both postural and smooth muscles, potentially resulting in muscle relaxation or ataxia [5]. These research findings align with existing literature [5], showing that all patients transitioned to lateral recumbency within 5 min of alpha-2 agonist administration. Additionally, decreased jaw tone and ease of mouth opening were observed in all patients. This suggests similar muscle effects of both medetomidine and dexmedetomidine.

As the hypnotic state deepens, the palpebral reflex typically slows down and eventually disappears under general anesthesia [3,9]. In this study, we observed that the palpebral reflex was present in all patients from both groups at T0. However, by T1, the palpebral reflex had disappeared, with 40% of patients in the 1st group and 60% in the 2nd group exhibiting this change. These findings are consistent with existing literature [3,9].

The corneal reflex is bilateral contraction of the orbicularis oculi muscle following corneal stimulation. Studies in animals and humans have shown that the corneal reflex is suppressed during sedation and anesthesia [21]. According to the results of this study, corneal reflexes were preserved in all patients at T0, whereas corneal reflexes were lost in 12% of the patients in the 1st group and 36% in the 2nd group at T1 following sedation. Although it has been argued that the corneal reflex does not disappear until deep anesthesia and is always present [17], the findings of the study are consistent with the existing data in the literature [21] and corneal reflexes were not obtained in 25% of the patients in the medetomidine group and 75% of the patients in the dexmedetomidine group after sedation.

Pupil size was assessed in 98 patients. However, 2 patients presented with chronic superficial keratitis (pannus), rendering the pupil invisible and therefore unable to be evaluated. While ocular reflexes are frequently employed to gauge the depth of anesthesia [13], we advocate for the use of objective CNS monitoring methods, particularly BIS, in patients with ocular issues. During the initial pupil assessment, 21.43% of patients exhibited normal pupil size, while 78.57% had mydriatic pupils. This contrasts with information in literature [35], which suggest that pupillary response during anesthesia is primarily influenced by premedication, with pupil dilation occurring due to excitement in non-premedicated animals, gradually narrowing during anesthesia. However, the results of this study revealed that mydriasis developed in patients following sedation. Previous studies have shown conflicting results regarding pupil diameter changes after administration of sedatives. One study in dogs reported a decrease in pupil diameter following medetomidine administration [22], while another study in cats reported an increase after a combination of medetomidine and ketamine [15]. The findings of this study contradicted the data

in the literature [22], while they were consistent with the data in the other literature [15]. Although it's known that opioid antagonists like butorphanol induce miosis in awake patients [16], none of our patients exhibited miosis after receiving butorphanol for preventive analgesia.

BIS 70-90 represents mild to moderate sedation and 60-70 represents deep sedation [26]. The mean BIS value at T1 was 72.82, which overlapped with the results of literature [26] and showed that the patients were in moderate conscious sedation. Medetomidine and dexmedetomidine are alpha-2 receptor agonists routinely used for sedation and analgesia. Dexmedetomidine causes weaker sedation and stronger antinociceptive effect than medetomidine [25,31]. In the intergroup evaluation, the mean BIS value of the 1st group was 72.82 and moderate sedation was observed according to source [26]. The mean BIS value of the 2nd group was 67.12, which indicates deep sedation according to the classification of source [26]. Intergroup BIS results showed that deeper sedation occurred in the dexmedetomidine group, contrary to the results of literature [31]. As a result of the BIS results, we think that dexmedetomidine will be more effective than medetomidine in procedures requiring procedural sedation by creating a hypnotic state close to general anesthesia.

In humans, moderate sedation is characterized by a reversible state where response to tactile and vocal stimuli remains intact [4,12]. However, when considering the results of BIS and LWR, it was observed that 72% of patients in the 1st group, classified under moderate sedation, exhibited a disappearance of the LWR reflex upon exposure to painful stimuli, which contradicts some existing literature [4,12]. This discrepancy might be attributed to the potent muscle relaxant and analgesic properties of medetomidine, without inducing loss of consciousness. Deep sedation, as defined in the literature [4,12], involves a reversible state where patients are less responsive to verbal stimuli and may require intervention to maintain airway patency, particularly after exposure to painful or repetitive stimuli. In the 2nd group, deep sedation was confirmed, with only 14% of patients displaying the LWR reflex, consistent with literature [4,12]. Moreover, this study results indicated a substantial decrease in response to painful stimuli among patients receiving dexmedetomidine, suggesting its greater nociceptive effect compared to medetomidine.

When the EMG falls below 40 units (1 bar), the BIS value is automatically recorded [28]. However, muscle activity may interfere with obtaining a reliable BIS reading [19]. In this study, the mean EMG values were 38.46% in the medetomidine group and 37.22% in the dexmedetomidine group. In both groups, we observed an appropriate EMG level, indicating that muscle activity decreased with sedation, consistent with existing literature [19,28], and reliable BIS data were automatically recorded. There was no significant difference between the medetomidine and dexmedetomidine groups when comparing EMG values in terms of muscle relaxation. However, upon analyzing LWR values, it appeared that the dexmedetomidine group exhibited stronger muscle relaxation compared to EMG levels.

It's been noted that relying solely on the BIS value is insufficient for effective sedation management [19]. A significant difference in BIS values was observed between patients with and without palpebral and corneal reflexes post-sedation. Specifically, the mean BIS value was 72.09 in animals exhibiting palpebral reflexes compared to 66.03 in those without, and 72.01 for patients with corneal reflexes compared to 63.5 in those without. While this suggests that palpebral and corneal reflexes may offer insight into the level of sedation, this study indicates that BIS provides a more accurate reflection of sedation status compared to physical examination results. Contrary to previous literature [19], it is argued that BIS can reflect a patient's sedation status more reliably than physical examination methods. This suggests the potential for developing a sedation scale in veterinary anesthesiology that incorporates both physical examination and BIS results.

The research conducted on rats and cats has demonstrated that alpha-2 adrenoceptor agonists induce mydriasis [30]. Moreover, there have been reports of myosis occurring in animals administered intravenous medetomidine [7]. In line with these results, which focused on alpha-2 adrenoceptor agonist administration, revealed mydriatic pupils in approximately 88% of the patients, consistent with the observations in source [30]. However, we did not observe myotic pupils, as reported by literature [7], in any of our patients. Statistically, we found no significant correlation between BIS and pupil size. This suggests that

pupil size may not be effective in determining sedation levels, contrary to common belief.

LWR, or the limb withdrawal reflex, is elicited by applying pressure to the interdigital skin in cats [8,35]. It typically results in limb retraction if anesthesia is insufficient [8]. However, the effect of sedation on LWR and its duration remain unclear [8,11]. In this study, we observed the disappearance of LWR in 79% of patients at T1. Among these, 36% were from the medetomidine group and 43% from the dexmedetomidine group. Simultaneously, we noted that patients with LWR had a mean BIS value of 75.52, whereas those without LWR had a mean BIS value of 68.49. This decrease in BIS value with deeper sedation levels suggests that LWR could serve as an indicator of sedation depth. Despite literature indicating uncertainty regarding the effects of sedation on LWR [8,11], according to the results of the study, it was found that the majority of sedated patients did not exhibit LWR. These findings suggest a positive correlation between LWR and sedation level.

CONCLUSION

BIS monitoring has proven to be an effective method for assessing sedation levels. While general anesthesia is often considered safer than sedation for minor interventional procedures in cats, we posit that controlled sedation with BIS monitoring can be safely employed in procedural sedation, emergency interventions for high-risk patients, and intensive care units. Although the effects of medetomidine and dexmedetomidine on reflexes used to monitor anesthesia depth have not been extensively reported in the literature, our study offers a comparative analysis of these commonly used alpha-2 agonists. We aimed to elucidate the effects of dexmedetomidine and medetomidine on reflexes. Our findings suggest that dexmedetomidine induces deeper sedation and proves more effective than medetomidine in procedural sedation, as supported by BIS and physical examination results.

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Ethical approval. The study was performed with approval from and under the guidelines of the University of Health Sciences Experimental Animals Local Ethics Committee (2019/109).

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

REFERENCES

1 **Bleijenberg E.H., Van Oostrom H., Akkerdaas L.C., Doornenbal A. & Hellebrekers L.J. 2011.** Bispectral index and the clinically evaluated anaesthetic depth in dogs. *Veterinary Anaesthesia and Analgesia*. 38(6): 536-543. DOI: 10.1111/j.1467-2995.2011.00651.X.

2 **Campagnol D., Teixeira Neto F.J., Monteiro E.R., Beier S.L. & Aguiar A.J. 2007.** Use of bispectral index to monitor depth of anesthesia in isoflurane-anesthetized dogs. *American Journal of Veterinary Research*. 68(12): 1300-1307. DOI: 10.2460/ajvr.68.12.1300.

3 **Clark L. 2009.** Monitoring the anaesthetised patient. In: Welsh L. (Ed). *Anaesthesia for Veterinary Nurses*. Singapore: Blackwell Publishing, pp.227-233.

4 **Cowles C.E. 2016.** Anestezi Aygıtları ve Monitörler, Morgan & Mikhail klinik anesteziyoloji. In: Morgan G.E., Mikhail M.S. & Murray M.J. (Eds). 5th edn. Ankara: Günes Tıp Kitabevleri, pp.9-123.

5 **Dugdale A.H., Beaumont G., Bradbrook C. & Gurney M. 2020.** Sedation and Premedication. In: *Veterinary Anaesthesia: Principles to Practice*. 2nd edn. Pondicherry: Wiley Blackwell, pp.55-77.

6 **Ebner L.S., Lerche P., Bednarski R.M. & Hubbell J.A. 2013.** Effect of dexmedetomidine, morphine-lidocaine-ketamine, and dexmedetomidine-morphine-lidocaine-ketamine constant rate infusions on the minimum alveolar concentration of isoflurane and bispectral index in dogs. *American Journal of Veterinary Research*. 74(7): 963-970. DOI: 10.2460/ajvr.74.7.963.

7 **Gomez M.M.I., Varela L.O., Fontalba N.J.L. & González C. 2020.** Effects of fentanyl on intraocular pressure and pupil size in medetomidine-methadone premedicated dogs: a pilot study. *Veterinary Record Open*. 7(1): e00039. DOI: 10.1136/vetreco-2019-000391.

8 **Hall L.W., Clarke K.W. & Trim C.M. 2001.** Principles and Procedures In: *Veterinary Anaesthesia*. 10th edn. London: W.B. Saunders, pp.240-247.

9 **Haskins S.C. 2015.** Monitoring anesthetized patients. In: Kurt A. Grimm K.A., Lamont L.A., Tranquilli W.J., Stephen A. Greene S.A., Sheilah A. & Robertson S.A. (Eds). *Veterinary anesthesia and analgesia, the fifth edition of Lumb and Jones*, Pondicherry: Wiley Blackwell, pp.86-113. DOI: 10.1002/9781119421375.ch4.

10 **Herbert G.L. & Murison P.J. 2013.** Eye position of cats anaesthetised with alfaxalone or propofol. *Veterinary Record*. 172(14): 365. DOI: 10.1136/vr.101404.

11 **Horsley K.T., Olby N.J., Mitchell M.A., Aulakh K.S. & Gines J. 2021.** Effect of sedation on the neurological examination of the patellar and withdrawal reflexes in healthy dogs. *Frontiers in Veterinary Science*. 8: 664150. DOI: 10.3389/fvets.2021.664150.

12 **İyilikçi L., Ökesli S. & Işık B. 2015.** Ameliyathane Dışı Anestezi Uygulamaları. *Türk Anesteziyoloji ve Reanimasyon Derneği TARD Anestezi Uygulama Kılavuzları*. pp.1-35.

13 **Kayhan Z. 2019.** İzlem, Ölçüm, Görüntüleme, Değerlendirme ve Kayıt Yöntemleri. In: *Klinik Anestezi*. 4. Baskı. İstanbul: Logos Yayıncılık Tic. A.Ş., pp.46-81.

14 **Kennedy M. J. & Johnson R.A. 2015.** Dexmedetomidine & Atipamezole. *Clinician Brief*. 2015: 65-67. Available at: https://www.cliniciansbrief.com/article/dexmedetomidine-atipamezole.

15 **Kibar M., Keskin A., Aymirzakizi A. & Öztürk Z. 2022.** Effects of medetomidine/ketamine and xylazine/ketamine anesthesia and their reversal by atipamezole on ocular parameters and monitored anesthesia care in cats. *Ankara Üniversitesi Veteriner Fakültesi Dergisi*. 69: 251-257. DOI: 10.33988/auvfd.869204.

16 **Larson M.D. 2008.** Mechanism of opioid-induced pupillary effects. *Clinical Neurophysiology*. 119(6): 1358-1364. DOI: 10.1016/j.clinph.2008.01.106.

17 **Lee L. 2018.** Anesthetic Monitoring. *Veterinary Surgery*. pp.1-11.

18 **March P.A. & Muir W.W. 2003.** Use of the bispectral index as a monitor of anesthetic depth in cats anesthetized with isoflurane. *American Journal of Veterinary Research*. 64(12): 1534-1541. DOI: 10.2460/ajvr.2003.64.1534.

19 **Medtronic. 2012.** Covidien BIS™ Bilateral Brain Monitoring Sensor. Available at: <https://www.medtronic.com/covidien/en-gb/products/brain-monitoring/bis-bilateral-sensor.html >

20 **Megda T.T., Sousa F.G., Miranda F.G., Barreto M.S.O., Mattoso C.R.S. & Beier S.L. 2022.** Echocardiographic assessment of felines sedated with dexmedetomidine or xylazine associated with butorphanol. *Research, Society and Development*. 11(12): e559111234902-e559111234902. DOI: 10.33448/rsd-v11i12.34902.

21 **Mourisse J., Gerrits W., Lerou J., Van Egmond J., Zwarts M.J. & Booij L.H.D.J. 2003.** Electromyographic assessment of blink and corneal reflexes during midazolam administration: useful methods for assessing depth of anesthesia? *Acta Anaesthesiologica Scandinavica*. 47(5): 593-600. DOI: 10.1034/j.1399-6576.2003.00100.x.

22 **Mrazova M., Rauser P., Burova J., Georgiou M. & Fichtel T. 2018.** Influence of medetomidine, acepromazine, fentanyl and butorphanol on intraocular pressure and pupil size in healthy dogs. *Veterinární Medicína*. 63(9): 413-419. DOI: 10.17221/51/2018-VETMED.

23 **Muir W.W. & Hubbell J.A. 2012.** Preanesthetic and Perioperative Medications. In: *Handbook of Veterinary Anesthesia*. Hoboken: Elsevier Health Sciences, pp.22-57.

24 **Murrell J. 2007.** Choice of premedicants in cats and dogs. *In Practice*. 29(2): 100-106. DOI: 10.1136/inpract.29.2.100.

25 **Paolo S. 2017.** Use of dexmedetomidine in veterinary practice. *International Journal of Clinical Anesthesiology*. 5(4): 1078.

26 **Pérez G.S., Lozano C.N., Ruiz Roca J.A., López J.P. & Gargallo Albiol J. 2020.** Evaluation of endovenous sedation using BIS monitoring in dentistry. A systematic review. *Medicina Oral, Patologia Oral y Cirugia Bucal*. 25(4): e439. DOI: 10.4317%2Fmedoral.22884.

27 **Rankin D.C. 2015.** Sedatives and tranquilizers. In: Kurt A. Grimm K.A., Lamont L.A., Tranquilli W.J., Stephen A. Greene S.A. & Sheilah A. Robertson S.A. (Eds). *Veterinary Anesthesia and Analgesia: the Fifth Edition of Lumb and Jones*. Pondicherry: Wiley Blackwell, pp.196-206. DOI: 10.1002/9781119421375.ch10.

28 **Saenubol P., Akatvipat A., Pleumsamran A. & Chankrachang S. 2021.** Correlation between bispectral index value and modified Glasgow Coma Scale score in dogs with altered level of consciousness. *Journal of Veterinary Emergency and Critical Care*. 31(1): 52-58. DOI: 10.1111/vec.13014.

29 Sager J. & McKune C.M. 2022. Anesthesia equipment and monitoring. In: Shelby A.M. & McKune C.M (Eds). *Small Animal Anesthesia Techniques*. 2nd edn. Hoboken: John Wiley & Sons, pp.28-52.

30 Schinetsky J. 2015. Effects of Medications on Pupillometry Measurements of Sedation in the Intensive Care Unit. *XULAneXUS*. 13(1): 3. Available at: <https://digitalcommons.xula.edu/xulanexus/vol13/iss1/3>.

31 Siegenthaler J., Pleyers T., Raillard M., Spadavecchia C. & Levionnois O.L. 2020. Effect of medetomidine, dexmedetomidine, and their reversal with atipamezole on the nociceptive withdrawal reflex in beagles. *Animals*. 10(7): 1240. DOI: 10.3390/ani10071240.

32 Simon B.T. & Steagall P.V. 2020. Feline procedural sedation and analgesia: when, why and how. *Journal of Feline Medicine and Surgery*. 22(11): 1029-1045. DOI: 10.1177/1098612X20965830.

33 Tranquilli W.J. & Grimm K.A. 2015. Introduction: use, definitions, history, concepts, classification, and considerations for anesthesia and analgesia. In: Kurt A. Grimm K.A., Lamont L.A., Tranquilli W.J., Stephen A. Greene S.A., Sheilah A. & Robertson S.A. (Eds). *Veterinary Anesthesia and Analgesia: The fifth edition of Lumb and Jones*. Pondicherry: Wiley Blackwel, pp.1-10. DOI: 10.1002/9781119421375.ch1.

34 Verma A., Sooryadas S., Dinesh P.T., Chandy G. & Caulkett N. 2020. Continuous rate infusion anaesthesia with dexmedetomidine-midazolam-ketamine-lignocaine in dogs. *Indian Journal of Veterinary Surgery*. 41(2): 104-106.

35 Vinerean H.V. 2018. Anesthesia Monitoring. Available at: < https://research.fiu.edu/ documents/facilities/acf/documents/anesthesia-monitoring-small-animals>.

36 Wagner M.C., Hecker K.G. & Pang D. S. 2017. Sedation levels in dogs: a validation study. *BMC Veterinary Research*. 13: 1-8. DOI: 10.1186/s12917-017-1027-2.