VETERINARSKI ARHIV 91 (6), 655-664, 2021 DOI: 10.24099/vet.arhiv.1112

Clinical evaluation of the intranasal administration of midazolam and reverse effects of flumazenil in Eurasian Buzzards (*Buteo buteo*)

Yusuf Altundag[1]*, Tugba Kurt[1], Serhat Özsoy[1], and İbrahim Altundag[2]

[1]*Department of Surgery, Faculty of Veterinary Medicine, University of Istanbul - Cerrahpasa, Avcilar, Istanbul, Turkey*

[2]*Department of Emergency Medicine, Haydarpaşa Numune Training and Research Hospital, University of Health Sciences, Üsküdar, Istanbul, Turkey*

ALTUNDAG, Y., T. KURT, S. ÖZSOY, İ. ALTUNDAG: Clinical evaluation of the intranasal administration of midazolam and reverse effects of flumazenil in Eurasian Buzzards (*Buteo buteo*). Vet. arhiv 91, 655-664, 2021.

ABSTRACT

Midazolam, the most commonly used drug in birds, has sedative, muscle relaxant, anxiolytic, amnestic, and appetite-enhancing effects. In this study, we aimed to reach the proper sedation level with intranasal (IN) administration of midazolam, and quick and safe recovery with intranasal flumazenil application after a certain period of time. The buzzards in the experiment reached the desired and controllable sedation at 6.7 ± 1.6 min after administration of IN midazolam at a dose of 2 mg / kg of body weight. In the saline group (%0.9 NaCl), the doses of midazolam and flumazenil calculated according to their weight were administered intranasally as 0.9% NaCl. The heart rate was 290.4 ± 17.81 and 294.8 ± 18.19 beats/min in the midazolam group, and 300.8 ± 17.76 beats/min in the saline group. Cloacal temperature was 41.42 ± 07, 41.39 ± 0.85 °C in the midazolam group and 41.6 ± 0.45 °C in the saline group. The respiratory rate was 48.8 ± 4.5, 47.1 ± 4.3 breaths/min in the midazolam group and 54.6 ± 2.7 breaths/min in the saline group. Flumazenil was used as an antagonist at 0.05 mg/kg intranasally, and after 14.1 ± 1.8 minutes the sedation effect disappeared. Then the buzzards returned to their standard behavior. In conclusion, we suggest IN use of midazolam and use of flumazenil for faster recovery in buzzards as a simple, fast, practical, and economical mode of sedation for minimally invasive procedures.

Key words: midazolam; intranasal administration; Eurasian buzzard; sedation

Introduction

Usually birds are held with bare hands or towels during diagnostic or therapeutic procedures, such as physical examination, blood collection, radiographic imaging, nail or beak trimming, and injections (DONELEY et al., 2006). Restraining them in this way often causes stress, increasing their respiratory rate and body temperature, and the result may be an injury to the bird, as well as a potentially hazardous situation for a handler (BLAS, 2015; DOSS and MANS, 2016). General anesthesia in birds predisposes them to cardiovascular and respiratory depression, and may lead to aspiration of stomach content, and hypothermia (ESCOBAR et al., 2016; SEOK et al., 2017).

*Corresponding author:
Yusuf Altundag, Faculty of Veterinary Medicine, University of Istanbul- Cerrahpasa, Department of Surgery, TR-34320 Avcilar, Istanbul - Turkey, E-mail: ysf.altundag@hotmail.com

ISSN 0372-5480
Printed in Croatia

Intranasal (IN) administration of sedative drugs is non-invasive, safe and painless, and has fewer complications than other routes of administration (OZBAY et al., 2015; KUBİAK et al. 2016; RAEİSİ et al., 2016). Midazolam, the most commonly used drug for birds, has sedative, muscle relaxant, anxiolytic, amnestic and appetite-enhancing effects (ARAGHİ et al., 2016). Recent studies have shown that the use of IN midazolam is suitable for short-term application (SCHAFFER et al., 2016; DOSS et al., 2018; NET et al., 2019).

As with other animals, Eurasian Buzzards require a maximum of 15 minutes of sedation in order to perform simple interventional procedures such as blood collection, injection or use of imaging devices such as X-rays. Quick onset of sedation and fast recovery is one of the most important features that drugs should have for sedation. We conducted this study on Eurasian Buzzards to determine the onset time of sedation after a new dosage and intranasal administration of midazolam, and to determine the recovery time from sedation with application of intranasal flumazenil after waiting for a certain period of time (approximately 15 min). After applying the flumazenil intranasally, we recorded the changes that occurred at one-minute intervals in the Eurasian buzzards, and the full recovery time from sedation. We compared the duration of action of midazolam and flumazenil with the intranasal administration of saline.

Materials and methods

This study on buzzards was approved by the Ethics Committee of Istanbul University for animal experiments local ethics on 31.05.2018, by decision number 2018/41, as a randomized controlled trial design. Twenty adult Eurasian buzzards (*B. buteo*) of unknown sex, weighing 0.9 to 1.03 kg were included in the study. The buzzards were sheltered at the wild animal treatment and rehabilitation unit (VAŞAK) of Cerrahpasa Veterinary Faculty of Istanbul University, Turkey, due to not being well enough to be released back into the wild (for coracoid fracture and luxations for example). One day before the study, clinical and parasitological examinations of the buzzards were performed. Fecal examination was performed with qualitative stool examination in all birds. Then, the birds were placed in metal cages measuring 50 × 49 × 35 cm in two groups and kept at a room temperature of 26 - 28 °C for local environment adaptation. The birds were fed with chicken meat and water.

Twenty minutes before commencement of the study, the respiratory and pulse rates of the birds were measured, and they were scored for in-cage parameters (Table 1). The animals were then held with a towel and handling gloves, and measurements were taken again. The birds were divided into two groups of 10 birds each. In Group 1 (midazolam), a 24 G IV catheter was inserted into each nostril and advanced approximately 4 mm, through which a 2 mg/kg dose of midazolam (Midolam, 5 mg/mL PHARMADA, Turkey), equally divided for each nostril, was administered. The birds were then returned to the cage. Physiological saline solution (0.9% NaCl, Osel, Turkey) was administered to the birds in Group 2 (control) using the same amounts and techniques as for Group 1. The birds were then returned to the cage. For the first 10 min, with the birds in cages, various parameters (head position, eyes, body position, response to a visual stimulation, response to auditory stimulation, and response to tactile stimulation) were assessed every minute (Table 1).

The parameters were scored according to the state of sedation, as 0 if awake, 1 if semi-sedated, and 2 if sedated at the desired level (Table 1). Ten minutes after the intranasal administration of midazolam, the birds were again caught with a towel and their movements were restricted for 5 min using the towel. During this period, the capturing (vocalization, defensive behavior, escape behavior, ease of capture) and restraining (vocalization/struggling) parameters were scored (Table 1). During sedation, at 5 min intervals, their respiratory rate/min was measured twice, cloacal temperature three times, and heart rate/min twice. Once the restraining time had ended, a 0.05 mg/kg dose of flumazenil (Fluxate 0.5 mg/5 ml, PHARMADA) was divided equally into two and administered intranasal into the nostrils. The birds were then returned to the cages.

Table 1. Sedation Scoring Scale to investigate the effects of IN Midazolam in Buzzards

Observation period	Behavior	Score		
		0	1	2
In cage	Head Position	Upright	Hanging	Beak/Head Resting on Floor
	Eyes	Open	Partially Closed	Completely Closed
	Body Position	Normal/Standing	Broad Based, Resting on Hocks	Sternally Recumbent
	Response to Visual Stimulation	Head and Eye movement and Vocalization	Reduced Head and Eye Movement	No Response
	Response to Auditory Stimulation	Head and Eye Movement and Vocalization	Reduced Head and Eye Movement	No Response
	Response to Tactile Stimulation	Head and Eye Movement and Vocalization	Reduced Head and Eye Movement	No Response
Capture	Vocalization	Normal/Screaming	Reduced/Chattering Reduction in Attempts or Magnitude of The Bird	Absent
	Defense Behavior	Attempting to Bite and Lunge At The Towel	Biting or Lunging at the towel	Absent
	Escape Behavior	Flying or Moving Away to Escape Capture By Towel	Reduced Attempts or Magnitude of Escape Behavior	Absent
	Ease of Capture	Flight in Response to Cage Attacking/Lunging at Towel	Attempted Flight or Hop/Jump; No or Mild Attempts to Attack/Lunge at Towel	No Flight or Jumping/Hopping and No Attempts to Attack/Lunge at Towel
Restraint	Vocalization/ Struggling	Normal/Screaming: Vigorous and Repetitive Movement of The Head, Legs, and Wings	Reduced/Chattering; Reduced Strength and frequency of The Head, Leg, and Wing Movement	Absent: No Head, Leg, or Wing Movement

After the administration of flumazenil, the in-cage parameters were scored again every minute, according to the state of sedation, until recovery (2: sedated, 1: semi-awake, 0: awake). A record was made for any bird that went back into a sedative state during the 60 min following administration of flumazenil.

Results

In all the birds in the experimental group, the intranasal sedative and antagonist administration was effective. Sedation caused no life-threatening complications in any of the birds. After intranasal administration of midazolam, it was determined that some of the anesthetic agent had been lost due to sneezing-like behavior in three of the 10 birds, and excessive wing fluttering in two birds.

The buzzards in the midazolam group weighed 1.2020 ± 0.167 kg and birds in the saline group weighed 1.136 ± 0.121 kg. After intranasal administration of midazolam, the desired level of sedation was achieved at 6.8 ± 1.6 min. For clinical examination 9.2 ± 1.6 min were required for the birds (Table 2). Sufficient sedation was maintained during this period (Fig. 3).

The heart rate was measured using a stethoscope, through auscultation by contact with the pectoral muscles of the birds for 1 min. Heart

Fig. 1. Intranasal administration of Midazolam into each nostril

Fig. 2. Birds observed, eyes partially closed

Table 2. Sedation onset times of buzzards and waiting times until flumazenil application

Animal number	Sedation Onset Time (min)	Remaining time for Clinical procedures (min)
1	6	10
2	6	10
3	10	6
4	5	11
5	5	11
6	8	8
7	8	8
8	6	10
9	8	8
10	6	10

Table 3. Heart rate, Respiratory rate and Cloacal temperatures in Midazolam group

	Heart Rates		Respiratory Rates		Cloacal Temperatures	
Animal Number	1st Measurement (beats/ min)	2nd Measurement (beats/ min)	1st Measurement breaths/ min)	2nd Measurement (breaths/ min)	1st Measurement (°C)	2nd Measurement (°C)
1	296	292	48	46	40	40
2	272	280	44	42	42	42
3	280	276	52	48	42	42
4	272	304	50	50	41	41
5	268	272	46	44	42	42
6	304	296	52	52	41	41
7	292	288	56	54	42	42
8	288	292	50	47	42	43
9	312	320	40	40	42	41
10	230	328	50	48	40	40
Mean ± SD	290·4 ± 1781	294·8 ± 1819	48.8 ± 4.5	47.1 ± 4.3	41.42 ± 0.7	41.39 ± 0.85

Table 4. Heart rate, Respiratory rate and Cloacal temperatures in Saline group

	Heart Rates	Respiratory Rates	Cloacal Temperatures
Animal number	Measurement (beats/min)	Measurement (breaths/min)	Measurement (°C)
1	308	56	41
2	284	52	42
3	288	56	42
4	328	56	42
5	276	50	42
6	308	54	41
7	300	58	42
8	292	54	42
9	324	58	42
10	300	52	41
Mean ± SD	300.8 ± 17.76	54.6 ± 2.6	41.7 ± 0.48

Table 5. After Administration of IN Midazolam time-dependent changes in the numbers of animals

After IN Midazolam Administration												
	Head Position		Eyes		Body Position		Response to Visual Stimulation		Response to Auditory Stimulation		Response to Tactile Stimulation	
Minutes	Score 1	Score 2	Score 1	Score 2	Score 1	Score 2	Score 1	Score 2	Score 1	Score 2	Score 1	Score 2
1. min	1	0	0	0	0	0	1	0	2	0	1	0
2. min	6	1	4	0	4	0	4	0	8	0	7	0
3. min	9	1	6	0	6	0	6	0	9	1	9	1
4. min	9	1	6	2	6	2	6	2	9	1	8	2
5. min	4	5	4	5	4	5	4	5	5	5	4	6
6. min	1	8	1	8	1	8	1	8	3	7	1	9
7. min	2	8	2	8	2	8	2	8	1	9	1	9
8. min	1	9	0	10	0	10	0	10	0	10	1	9
9. min	1	9	0	10	0	10	0	10	0	10	0	10
10. min	1	9	0	10	0	10	0	10	0	10	0	10

Table 6. After Administration of IN Flumazenil time- dependent changes in the numbers of animals

After IN Flumazenil Administration												
	Head position		Eyes		Body position		Response to visual Stimulation		Response to auditory Stimulation		Response to tactile Stimulation	
Minutes	Score 1	Score 0	Score 1	Score 0	Score 1	Score 0	Score 1	Score 0	Score 1	Score 0	Score 1	Score 0
1. min	3	0	3	0	3	0	3	0	3	0	3	0
2. min	4	1	4	1	2	1	6	0	6	0	6	0
3. min	9	1	9	1	6	4	9	0	8	1	9	1
4. min	8	2	8	2	6	4	8	1	8	1	9	1
5. min	8	2	8	2	1	9	8	2	8	1	9	1
6. min	8	2	8	2	1	9	8	2	8	1	8	2
7. min	7	3	7	3	1	9	7	3	8	1	8	2
8. min	5	5	5	5	1	9	7	3	9	1	6	4
9. min	3	7	3	7	0	19	4	6	9	1	6	4
10. min	1	9	1	9			4	6	8	2	3	7
11. min	1	9	1	9			3	7	5	5	3	7
12. min	0	10	0	10			3	7	4	6	2	8
13. min							3	7	3	7	0	10
14. min							2	8	1	9		
15. min							1	9	1	9		
16. min							1	9	1	9		
17. min							0	10	1	9		
18. min									0	10		

Fig. 3. Eyes closed, sternal recumbency, buzzard under desired sedation

rate was measured twice upon capturing the birds in Group 1 (Table 3). The mean heart rate in this group was 294.8 beats/min. In Group 2, heart rate was measured only once to reduce stress (Table 4). The mean heart rate in this group was 304.0 beats/min. The respiratory rate was measured using direct inspection of pectoral muscles.

Respiratory rates in Group 1 were measured twice upon capturing the birds (Table 3).

In Group 2, respiratory rates were 54.6 ± 2.6 breaths/min. Cloacal temperature was measured in Celsius by a digital pediatric thermometer. A probe was placed in the cloaca at a depth of 1-2 cm. During sedation, measurements were taken twice at an interval of 40 - 60 sec (Table 3), and mean temperatures were 41.42, 41.39 and 41.28 °C. In Group 2, temperatures were 41.7 ± 0.48 °C (Table 4).

The mean time between intranasal midazolam and flumazenil was 9.2 min. After administration of flumazenil, the birds were placed in normal posture positions at 14, 17, 12, 14, 14, 11, 15, 13, 15 and 6 minutes, respectively. The mean duration was calculated as 13.1 minutes. No complications were seen in recovery from sedation.

The results were evaluated in three stages: intranasal administration of midazolam; latency of sedation, desired duration of sedation and administration of intranasal flumazenil; and the time taken to recover from sedation. The parameters were scored according to the latency of sedation, as 1 and 2. The number of birds in which sedation was achieved was determined on the basis of this assessment (Table 5). In the second part of the evaluation, vocalization, defensive behavior, escape behavior, ease of capture, and vocalization/struggling behavior were scored based on observations during capturing and restraining. Each of these parameters scored 2 points, indicating the presence of the desired sedation. In the third part of the evaluation, the observation parameters were measured again when the birds had been returned to their cages, and recovery time from anesthesia was determined (Table 6).

SPSS for Windows (SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. Differences in time-dependent changes were evaluated using the Friedman test for non-parametric and repeated measurements. For subgroups with significant differences, the Wilcoxon signed-ranks test was used to determine which measurement times caused the significant difference. Statistical significance was set at $P<0.05$.

For the body position parameter, the effect of measurement time was statistically non-significant after 5 min. Following intranasal administration of flumazenil, there was no statistical significance after 6 min.

For the response to tactile stimulation parameter, the measurement time did not have a significant effect 6 min after administration of midazolam, and after 10 min after the administration of flumazenil.

For the response to auditory stimulation, the effect of measurement time was not significant after 6 min before and 13 min after the intranasal administration of flumazenil.

For evaluation of response to a visual stimulation, the measurement time did not have a statistically significant effect after 5 min before and after 11 min following the administration of flumazenil.

In assessment of the eyes, there was no statistically significant difference after 6 min. Following the administration of flumazenil, no significance was found after 5 min.

Following the intranasal administration of midazolam, all parameters were statistically significantly different after 5 min, compared to baseline values.

After the administration of flumazenil, statistically significant differences to baseline values were obtained after 6 min for head position, 3 min for eyes, 5 min for body position, 9 min for response to a visual stimulant, 11 min for response to sound, and 10 min for response to touch.

Discussion

As reported in other birds, the nasal tract provides rapid absorption and short-term sedation latency, due to the rich vascular network and high permeability (HEARD, 1997; FORBES, 1998; HORNAK et al., 2015).

In studies investigating the IN administration of midazolam at the same dose, the mean latency of sedation was reported as 5.4 ± 1.2 min and 5.1 ± 0.9 min for blue-fronted and orange-winged Amazon parrots, respectively (SCHAFFER et al., 2017). In addition, in other midazolam studies performed at different doses in different species, sedation latency was determined as 1.3 ± 0.44 min in budgerigars (SADEGH, 2013), 1.02 ± 0.29 min in finches (BIGHAM and MOGHADDAM, 2013), and 1.9 ± 1.0 min in canaries (VESAL and ZARE, 2006). In the present study, mean latency of sedation was 6.8 min and sedation latency was 1 min. These durations are similar to those reported for the Hispaniolan parrot (MANS et al., 2012). In a study of Hispaniolan parrots, following intranasal administration of midazolam, partial or complete closure of the eyelids, standing or broad-based body position or pressing on the tarsal joint were observed (MANS et al. 2012). Partial or complete closure of the eyelids and sternal posture were observed in the birds in our study.

Dorsal recumbency was not observed after midazolam administration in parrots (SCHAFFER et al. 2017), but was reported in canaries (SADEGH, 2013) and pigeons after the intranasal administration of midazolam and diazepam (MOGHADAM et al., 2009), and in finches after midazolam alone (BİGHAM and MOGHADDAM, 2013). In the present study, dorsal recumbency occurred in all the birds after administration of intranasal midazolam.

Canaries (VESAL and ZARE, 2006), budgerigars (SADEGH, 2013), and Canada geese (VALVERDE et al., 1990) were reported to have slightly reduced respiratory rates after the IN administration of midazolam. In contrast, Hispaniolan parrots did not show any signs of respiratory distress during sedation (MANS et al., 2012). In our study, there was a minimal decrease in the respiratory rate of the sedated animals.

Cloacal temperature was 41.2 ± 0.1 °C in healthy buzzards (KILIC and PASA, 2009). In the present study, cloacal temperature in the saline group was 41.6 °C, which was similar to that in other published studies.

In a study comparing propofol and a midazolam-ketamine combination in buzzards, cloacal temperatures were 40.3 ± 0.6 and 40.9 ± 0.2 °C, respectively (KILIC and PASA, 2009). In our study, we recorded cloacal temperatures of 41.42, 41.39, and 41.28 °C, respectively.

In healthy birds, the heart rate has been reported to be 353 ± 44 beats/min (STRAUB et al., 2003). Similarly, in our study, the mean heart rate in the saline group was 304.8 beats/min.

As recently reported, the heart rate of buzzards was 243 ± 20 beats/min under isoflurane anesthesia (KILIC and PASA, 2009) and 342.5 ± 12.3 beats/min, 10 min after intravenous administration of propofol (STRAUB et al., 2003). In our study, the heart rate was 290.4 beats/min and 294.8 beats/min in midazolam group, respectively.

Previous studies have reported complications, such as myoclonic convulsions (SADEGH, 2013; BIGHAM and MOGHADDAM, 2013), nasal discharge, and vomiting after IN midazolam administration (VESAL and ESKANDARİ, 2006; VESAL and ZARE, 2006). In the present study, no clinical side effects such as convulsion, serous nasal discharge, or vomiting were observed. In addition, the birds displayed a behavior of rhythmically moving their heads from one side to the other, as if following a moving object. This finding has not been previously reported in the literature. This movement disorder with rotatory character in some Buzzards was considered to be a temporary complication of midazolam administration in the sedative period. Therefore, this complication was considered as a side effect of midazolam.

The effect of sedation was reported to last for 2 - 3 h in parakeets (VESAL and ESKANDARİ, 2006), 25.6 ± 5.7 min in blue-fronted Amazon parrots, and 27.1 ± 3.7 min in orange-winged Amazon parrots (SCHAFFER et al., 2017). Since this is too long for simple clinical examinations and procedures in buzzards, we used flumazenil at a dose of 0.05 mg/kg, as an antagonist of midazolam.

In a study evaluating quails, the effect of midazolam followed by a single-dose injection of flumazenil, after the intramuscular administration of midazolam, was found to disappear in less than 2 min (DAY and ROGE, 1996). In the present study, midazolam lost its effect within 13.1 min after the IN administration of flumazenil.

In conclusion, IN administration of midazolam at a dose of 2 mg/kg had a mild to moderate sedative effect, resulting in short sedation latency and rapid recovery after flumazenil administration. Sedation sufficient for clinical evaluation was successfully achieved in all birds. Intranasal use of an antagonist, flumazenil, at a dose of 0.05 mg/kg, assisted in the rapid recovery from sedation. Deep sedation or excitation was not observed in any bird. For these reasons, we suggest the use of intranasal midazolam in buzzards as a simple, fast, practical and economical form of sedation in minimally invasive procedures.

References

ARAGHI, M., S. AZIZI, N. VESAL, B. DALIR- NAGHADE (2016): Evaluation of the sedative effects of diazepam, midazolam, and xylazine after intranasal administration in juvenile ostriches (*Struthio camelus).* J. Avian. Med. Surg. 30, 221-226.

DOI: 10.1647/2015-110

BIGHAM, A. S., Z. MOGHADDAM (2013): Finch (*Taeneopygia guttata*) sedation with intranasal administration of diazepam, midazolam or xylazine. J. Vet. Pharmacol. Ther. 36, 102-104.

DOI: 10.1111/j.1365-2885.2009.01102.x

BLAS, J. (2015): Stress in birds. In: Sturkie's Avian Physiology. (Scanes, C. G Ed.), Academic Press, Waltham, MA, pp. 769-810.

DAY, T. K., C. K. ROGE (1996): Evaluation of sedation in quail induced by use of midazolam and reversed by use of flumazenil. J. Am. Vet. Med. Assoc. 209, 969-971.

DONELEY, B., G. J. HARRISON, T. L. LIGHTFOOT (2006): Maximizing information from the physical examination. In: Clinical Avian Medicine. Vol I. (Harrison G. J., T. L. Lightfoot, Eds.), Spix Publishing, Palm Beach, Florida, pp.154-212.

DOSS, G. A., D. M. FINK, C. MANS (2018): Assessment of sedation after intranasal administration of midazolam and midazolam-butorphanol in cockatiels (*Nymphicus hollandicus*). Am. J. Vet. Med. Res. 79, 1246-1252.

DOI: 10.2460/ajvr.79.12.1246

DOSS, G. A., C. MANS (2016): Changes in physiologic parameters and effects of hooding in red-tailed hawks (*Buteo jamaicensis*) during manual restraint. J Avian Med Surg. 30, 127-132.

DOI: 10.1647/2015-096.

ESCOBAR, A., R. W. ROCHA, B. H. PYPENDOP, D. Z. FILHO, S. S. SOUSA, C. A. VALADAO (2016): Effects of methadone on the minimum anesthetic concentration of isoflurane, and its effects on heart rate, blood pressure and ventilation during isoflurane anesthesia in hens (*Gallus gallus domesticus*). Plos One.11, e0152546.

DOI: 10.1371/journal.pone.0152546

FORBES, N. A (1998): Avian anesthesia. Vet Q. 20, 65-66.

DOI: 10.1080/01652176.1998.10807418

HEARD, D. J (1997): Anesthesia and analgesia. In: Avian Medicine and Surgery.(Altman, R. B., S. L. Clubb, G. M. Dorrestein, Eds.), WB Saunders Co, Philadelphia Pennsylvania, pp. 807-827.

HORNAK, S., T. LIPTAK, V. LEDECKY, R. HROMADA, J. BILEK, J. MAZENSKY, D. PETROVIC (2015): A preliminary trial of the sedation induced by intranasal administration of midazolam alone or in combination with dexmedetomidine and reversal by atipamezole for a short-term immobilization in pigeons. Vet. Anaesth. Analg. 42, 192-196.

DOI: 10.1111/vaa.12187

KILIC, N., S. PASA (2009): Cardiopulmonary effects of propofol compared with those of a medetomidine-ketamine combination in the common buzzards (*Buteo buteo*). Rev. Med. Vet. 160, 154-159

KUBIAK, M., L. ROACH, K. EATWELL (2016): The influence of a combined butorphanol and midazolam pre-medication on anesthesia in psittacid species. J. Avian. Med. Surg. 30, 317-323.

DOI: 10.1647/2013-072

MANS, C., D. S. GUZMAN, L. L. LAHNER, J. PAUL-MURPHY, K. K. SLADKY (2012): Sedation and physiologic response to manual restraint after intranasal administration of midazolam in hispaniolan amazon parrots (*Amazona ventralis*). J. Avian. Med. Surg. 26, 130-139.

DOI: 10.1647/2011-037R.1

MOGHADAM, A. Z., A. B. SADEGH, S. SHARIFI, S. HABIBIAN (2009): Comparison of intranasal administration of diazepam, midazolam and xylazine in pigeons: clinical evaluation. Iran J Vet Res. 1, 12-26.

NET, R. L., D. M. MULCAHY, A. SANTAMARIA-BOUVIER, S. G. GILLIAND, T. D. BOWMAN, C. LEPAGE, S. LAIR (2019): İntranasal administration of midazolam hydrochloride improves survival in female surf scoters (*Melanitta Perspicillata*) surgically implanted with intracoelomic transmitters. J. Zoo Wildlife Med. 50, 167-175.

DOI: 10.1638/2018-0115

OZBAY, I., C. KUCUR, A. DEGER, I. ITAL, C. M. KASIM, F. OGHAN (2015): Cytotoxic effects of intranasal midazolam on nasal mucosal tissue. J. Craniofac. Surg. 26, 2008-2012.

DOI: 10.1097/SCS.0000000000001965

RAEISI, A., M. TAATI, M. ROSTAMI, E. HAJITABAR (2016): Anesthesia and sedation in chough (*pyrrhocorax pyrrhocorax*) following intranasal administration of diazepam, midazolam, xylazine with or without ketamine: clinical evaluation. Iran J. Vet. Surg. 11, 23-27.

SADEGH, A. B (2013): Comparison of intranasal administration of xylazine, diazepam, and midazolamin in Budgerigars (*Melopsittacus undulatus*): clinical evaluation. J. Zoo Wildlife Med. 44, 241-244.

DOI: 10.1638/2009-0116R3.1

SCHAFFER, D. P. H., N. L. L. C. ARAUJO, A. C. S. RAPOSA, E. F. M. FILHO, J. V. R. VIEIRA, A. P. ORIA (2017): Sedative Effects of İntranasal Administration in Wild Caught Blue-fronted Amazon (*Amazona aestiva*) and Orange-winged Amazon (*Amazona amazonica*) parrots. J Avian Med. Surg. 31, 213-218.

DOI: 10.1647/2016-201

SCHAFFER, D., A. RAPOSA, F. LIBORIO, R. SILVA, N. ARAUJO, A. ORIA (2016): Intranasal administration of midazolam in blue-and-yellow macaws (*Ara araruana*): evaluation of sedative effects. Vet. Anaesth. Analg. 43, 459-460.

DOI: 10.1111/vaa.12355

SEOK, S. H., D. H. JEONG, I. H. HONG, H. C. LEE, S. C. YEON (2017): Cardiorespiratory dose-response relationship of isoflurane in Cinereous vulture (*Aegypius monachus*) during spontaneous ventilation. J. Med. 79, 160-165.

DOI: 10.1292/jvms.16-0314

STRAUB, J., FORBES, A. N., THİELEBEİN, J., PEES, M (2003): The effects of isoflurane anaesthesia on some Doppler-derived cardiac parameters in the common buzzard (*Buteo buteo*). Vet. J. 166, 273-276.

DOI: 10.1016/s1090-0233(03)00074-1

VALVERDE, A., V. L. HONEYMAN, D. DYSON, A. E. VALLİANT (1990): Determination of a sedative dose and influence of midazolam on cardiopulmonary function in Canada geese. Am. J. Vet. Res. 51, 1071-1074

VESAL, N., M. H. ESKANDARİ (2006): Sedative effects of midaz,olam and xylazine with or without ketamine and detomidine alone following intranasal administration in ring-necked parakeets. J. Am. Vet. Med. Assoc. 228, 383-388.

DOI:10.2460/javma.228.3.383

VESAL, N., P. ZARE (2006): Clinical evaluation of intranasal benzodiazepines, alpha-agonists and their antagonis ts in canaries. Vet. Anaesth. Analg. 33, 143-148.

DOI: 10.1111/j.1467-2995.2005.00244.x

Received: 18 May 2020
Accepted: 22 October 2020

ALTUNDAG, Y., T. KURT, S. ÖZSOY, İ. ALTUNDAG: Klinička procjena intranazalne primjene midazolama i reverzibilnih učinaka flumazenila u euroazijskog škanjca običnog (*Buteo buteo*). Vet. arhiv 91, 655-664, 2021.

SAŽETAK

Midazolam, koji se najčešće upotrebljava u ptica, ima sedativni učinak, miorelaksans je, anksio-litik, amnestik te poboljšava apetit. U ovom se istraživanju nastojala postići odgovarajuća sedacija intranazalnom primjenom (IN) midazolama te brz i siguran oporavak primjenom intranazalnog flumazenila poslije određenog vremena. U škanjaca je postignuta željena sedacija 6,7 ± 1,6 minuta poslije intranazalne primjene midazolama u dozi od 2 mg/kg tjelesne mase. U skupini kojoj je da-vana fiziološka otopina (0,9%-tni NaCl), doze midazolama i flumazenila izračunate su prema tjelesnoj masi jedinki i primijenjene intranazalno kao 0,9%-tni NaCl. Srčani su otkucaji bili 290,4 ± 17,81 i 294,8 ± 18,19 u minuti u skupini s midazolamom i 300,8 ± 17,76 otkucaja u minuti u skupini s fiziološkom otopinom. Temperatura kloake bila je 41,42 ± 0,7, 41,39 ± 0,85 °C u skupini s midazolamom i 41,6 ± 0,45 °C u skupini s fiziološkom otopinom. Brzina disanja bila je 48,8 ± 4,5, 47,1 ± 4,3 udaha u minuti u skupini s midazolamom i 54,6 ± 2,7 u skupini koja je dobivala fiziološku otopinu. Flumazenil je primijenjen kao antagonist u dozi od 0,05 mg/kg intranazalno, a poslije 14,1 ± 1,8 minuta sedativni je učinak nestao. Nakon toga škanjci su se uobičajeno ponašali. Zaključeno je da se intranazalna primjena midazolama i flumazenila za brz oporavak može pre-poručiti u škanjaca kao jednostavan, brz, praktičan i ekonomičan postupak sedacije u minimalnoinvazivnim zahvatima.

Ključne riječi: midazolam; intranazalna primjena; euroazijski škanjac obični; sedacija