Effects of Midazolam and Midazolam-Butorphanol on Gastrointestinal Transit Time and Motility in Cockatiels (Nymphicus hollandicus)

Authors: Martel, Anna, Mans, Christoph, Doss, Grayson A., and Williams, Jackie M.

Source: Journal of Avian Medicine and Surgery, 32(4) : 286-293

Published By: Association of Avian Veterinarians

URL: https://doi.org/10.1647/2017-266

Journal of Avian Medicine and Surgery 32(4):286–293, 2018

Original Study

Effects of Midazolam and Midazolam-Butorphanol on Gastrointestinal Transit Time and Motility in Cockatiels (*Nymphicus hollandicus*)

Anna Martel, DVM, Christoph Mans, Dr med vet, Dipl ACZM, Grayson A. Doss, DVM, Dipl ACZM, and Jackie M. Williams, DVM, MS, Dipl ACVR

Abstract: Positive contrast gastrointestinal (GI) studies are performed frequently in avian medicine to identify GI obstruction, luminal distension, and intracoelomic mass effects. However, repeated manual restraint and radiographic positioning may result in a stress-response and associated morbidity in birds, which can be attenuated by administration of sedative drugs. In mammals, many sedative drugs have been shown to affect GI transit times and motility. In this randomized, blinded, controlled prospective study, the effects of midazolam (M; 6 mg/kg IM) and midazolam-butorphanol (MB; 3 mg/kg each IM) on GI transit times were evaluated in 12 healthy cockatiels (*Nymphicus hollandicus*). Iohexol (20 mL/kg) was administered by crop gavage 15 minutes after induction of sedation, and fluoroscopic images were obtained at different time points. Both sedation protocols significantly affected GI transit times and motility, and the MB protocol had more pronounced effects. Overall median (range) GI transit times were 60 (30–120), 90 (30–120), and 120 (120–180) minutes for the control, M, and MB groups, respectively. Ventricular contractions were markedly reduced with both sedation protocols, while esophageal boluses were reduced only in the MB group. Visualization of the GI tract after iohexol administration was graded highest in the control group and poorest in the MB group. Our results show that commonly used sedative drugs have significant effects on GI transit time and motility in birds. Therefore, GI transit times obtained in sedated birds should not be compared to available reference transit times obtained from unsedated animals.

Key words: sedation, midazolam, butorphenol, GI, gastric, contrast, iohexol, barium, imaging, avian, cockatiel, *Nymphicus hollandicus*

Introduction

Positive contrast gastrointestinal (GI) studies are performed frequently in avian medicine to identify GI obstruction, luminal defects and distension, and intracoelomic mass effects.[1–3] Furthermore, evaluation of ventricular and small intestinal motility, filling and emptying of individual GI segments with contrast material, and overall GI transit time can aid in the diagnosis of GI motility disorders. In birds, GI hypomotility can be observed with many pathologic processes, including heavy metal toxicosis, gastrointestinal parasitism, and inflammation.[1] Positive-contrast medium is administered typically via gavage to reduce the risk of aspiration, and radiographic exposures are taken at various time points after gavage to assess target organs or follow progression of contrast medium through the GI tract. Only a few studies have examined GI transit times in psittacine birds, including African grey parrots (*Psittacus erithacus*), *Amazona* species parrots, and an umbrella cockatoo (*Cacatua alba*).[2,4–6] While cockatiels (*Nymphicus hollandicus*) are among the most common pet birds, no normal GI transit times have been reported for this species.

Manual restraint is used commonly in veterinary practice to facilitate radiographic positioning for the repeated radiographic exposures needed for

From the University of Wisconsin-Madison, School of Veterinary Medicine, Department of Surgical Sciences, 2015 Linden Drive, Madison, WI, 53706 (Martel, Mans, Doss); and Northstar VETS, 315 Robbinsville-Allentown Road, Robinsville, NJ, 08691, USA (Williams).

traditional GI contrast studies. However, the stress induced with manual restraint may result in undesirable effects, such as hyperthermia or tachypnea, as well as decompensation in critically ill birds.[1,4,6–9] Sedation has become more common in avian practice to attenuate the stress response caused by manual restraint and to facilitate various diagnostic and therapeutic procedures.[8] Midazolam and butorphanol currently are the sedative drugs used most commonly in birds.[10] While sedation is beneficial for minimizing stress and facilitating positioning when performing diagnostic imaging, it also may have significant effects on GI transit times and motility in birds, as demonstrated in mammals.[11–19] Benzodiazepines have varying effects on the GI tract, depending on species. Midazolam significantly delays GI transit and gastric emptying in mice.[13] Diazepam increases gastric emptying time in cats, while it decreases gastric emptying time in people.[17,20] This divergence in effects further highlights the necessity for species–specific and dose-specific studies. Conversely, opioid drugs consistently increase GI transit time in people.[15,21–24] Butorphanol, specifically, prolongs GI transit time in dogs, ponies, and horses.[11,14,25] Currently, there are no published studies investigating the effects of drugs used for sedation on GI motility and transit times in birds. Therefore, the objective of this study was to examine the effect of two sedation protocols (midazolam vs midazolam-butorphanol) on GI transit time and motility in cockatiels. Our hypotheses were that both protocols would have a significant effect on GI transit times and motility, and the midazolam-butorphanol protocol would have more pronounced effects.

Materials and Methods

Animals

This study was approved by the Institutional Animal Care and Use Committee, School of Veterinary Medicine, University of Wisconsin-Madison. Adult cockatiels (N = 12; 6 female, 6 male) less than 4 years old were obtained from a breeder for use in this study. Median body weight was 97 g (range, 80–110 g). Birds were housed adjacently in wire enclosures (76 × 46 × 46 cm) in groups of 3 (same sex groups). Cockatiels were allowed to acclimate for 2 weeks before the beginning of the experiments. Animals were housed in a climate-controlled room with a room temperature of 22°C to 24°C (71°F–75°F), relative humidity of 40% to 55%, and a 12 : 12-hour, light : dark cycle. A seed mix diet obtained from the breeder was fed as the primary diet and a cuttlefish bone was available in each cage. Millet sprigs and a seed-based commercial diet (Nutriberries, Lafeber Co., Cornell, IL, USA) also were offered two to four times per week. Various toys were provided for enrichment. Physical examination, packed cell volume, estimated white blood cell counts, and fecal parasitologic examinations performed before starting the experimental trials revealed no significant abnormalities, and all birds were considered to be in good health.

Study design and procedures

To determine the effects of sedation on GI transit time in cockatiels, the birds were assigned to three treatment groups in a randomized, complete crossover design: (1) midazolam (M) group, which was administered 6 mg/kg midazolam intramuscularly (IM); (2) midazolam-butorphanol (MB) group, which was administered 3 mg/kg midazolam and 3 mg/kg butorphanol IM as a single injection; and (3) control group (C), which was administered 0.1 mL lactated Ringer's solution (LRS) IM. The volume of LRS administered to the control group was the approximate average of volumes administered to birds in the M and MB groups. Injections in all groups were administered in the pectoral musculature. The design of the complete crossover was such that each bird was represented in all three treatments (M, MB, and C) in a randomized sequence.

On each day of the experimental trials, animals were fasted for 60 minutes before IM sedative drug administration. Fifteen minutes after sedation, iohexol (20 mL/kg; Omnipaque 300 mg/mL, GE Healthcare, Marlborough, MA, USA) was administered by crop gavage using a 16-gauge, curved, ball-tipped metal gavage needle placed at the level of the sternal notch. The iohexol dose used in this study was determined in preliminary studies (data not shown) to result in sufficient visualization of the GI tract when compared to lower doses (5 and 10 mL/kg). All trials were started between 8 and 10 AM.

After completing the fluoroscopic studies, birds in the M and MB groups received flumazenil (0.05 mg/kg IM) to reverse any remaining sedative effects of midazolam. Birds in the control group did not receive flumazenil after imaging. The butorphanol was not reversed. After administration of flumazenil, birds were returned to their enclosures and monitored until fully recovered. A minimum washout period of 7 days was allotted between trials.

For fluoroscopic image acquisition, cockatiels were placed in custom-made, ventilated enclosures measuring 23.5 × 10 × 8 cm, constructed from opaque, white, corrugated plastic sheets. Fluoroscopy was performed with a commercial C-arm unit (OEC 8900 C-arm; General Electric, Fairfield, CT, USA). Exposure factors were automatically adjusted by the unit and not recorded.[5,6,26] Right lateral and ventrodorsal views were taken at –5, 5, 15, 30, 60, 120, and 180 minutes after administration of iohexol. At the 30- and 60-minute time points, 60 seconds of video (15 frames per second) were recorded using the right lateral view to assess crop and ventricular contraction rates. If the contrast media had reached the cloaca after 60 minutes, but before the 180-minute mark, no further images were acquired.

After acquisition, fluoroscopic images and videos were reviewed by a single observer (AM), blinded to the identity and treatment group of the birds. Times required for contrast media to reach the proventriculus, ventriculus, intestines, and cloaca in each trial were evaluated. Overall GI transit time was defined as the time to presence of contrast material within the cloaca or time to defecation of contrast media. Video sequences were reviewed for calculation of esophageal bolus and ventricular contraction rates per minute. No retroperistalsis was observed aborad to the esophagus. The retroperistalsis observed in the esophagus was considered minimal and not quantified.

Visualization of the amount of contrast media present within the ventriculus and intestine was graded as poor (0), moderate (1), or excellent (2) using still fluoroscopic images at the time point at which the overall GI transit time had occurred (Fig 1). A poor score (0) indicated limited intestinal and ventricular filling and inconsistently defined luminal margins of the intestines. A moderate score (1) was characterized by more distinct margins and increased filling with contrast, but the ventriculus and intestines were not completely outlined. An excellent score (2) was allotted when the ventriculus and intestines were clearly filled and the lumen clearly outlined with contrast.

Data analysis

Data were analyzed by using a commercial statistical software package (SigmaPlot, version 12.5; Access Softek, Berkeley, CA, USA). The data were tested for normality by a Shapiro-Wilk test and for constant variance by the Brown-Forsythe test. Data were transformed before further analysis, if necessary. Repeated measures analysis of variance (ANOVA) or Friedman ANOVA on ranks were used to analyze the data for the effects of the drug protocol used on GI transit times and motility and visualization scores. The Holm-Sidak method or Student-Newman-Keuls method was used for post hoc pairwise multicomparison procedures. Data are reported as mean and standard deviation (SD) or as median and range unless otherwise specified. $P < .05$ was considered significant.

Results

Both sedation protocols resulted in a significant increase in overall GI transit time (Table 1). The effects of MB were more pronounced, and a significant delay in contrast media reaching the ventriculus and the intestine also occurred in this group (Table 1). Midazolam administered alone had less pronounced effects on GI transit times, and the differences from the control group were not clinically or statistically significant except for the increase in overall GI transit time.

Esophageal bolus frequencies did not differ between the control and midazolam groups (Table 2) at 30 and 60 minutes after contrast media administration. In the MB group, the esophageal bolus frequency was lower at both time points and significantly lower at 60 minutes compared to the other two groups (Table 2). Ventricular contractions were significantly reduced with both sedation protocols compared to the control group (Table 2).

Visualization of the ventriculus and intestine were scored significantly lower in the MB (median score 0, range 0–1) compared to the control (median score 2, range 1–2) and M (median score 1, range 0–1) groups. The visualization scores were significantly lower in the M than in the control groups.

Discussion

As hypothesized and comparable to findings in mammalian species, sedation protocols of midazolam alone and midazolam-butorphanol resulted in a significant delay of GI transit times in cockatiels.[16,18,25] Delayed GI transit time was more significant with the MB protocol. Administration of midazolam alone resulted in clinically and statistically less significant effects. Overall GI transit times were increased in 5/12 birds in the M group and in 10/12 in the MB group compared to the control group.

These results were similar to studies performed in mammals. In dogs, butorphanol (0.05 mg/kg) in combination with acepromazine (0.1 mg/kg) de-

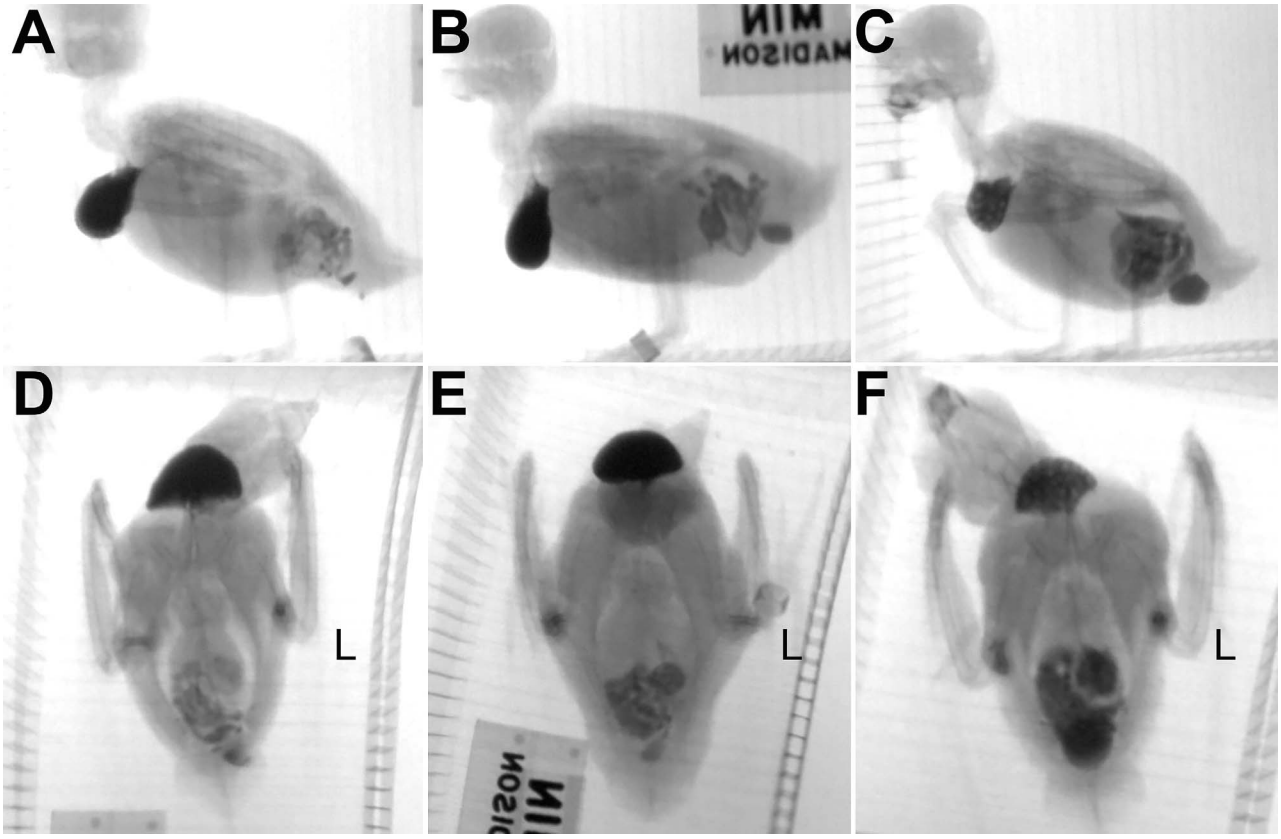

Figure 1. Differences in visualization of orally administered iohexol (20 mL/kg) in healthy cockatiels on lateral and dorsoventral fluoroscopic images. The visibility of the amount of contrast media present within the ventriculus and intestine was scored as poor (0; A, D), if the intestine and ventricular filling was poor and margins of the intestine were inconsistently defined. A moderate visualization score (1; B, E) was given if the GI tract margins were more distinct (ventriculus and intestines were less completely outlined). An excellent visualization score (2; C, F) was given if the ventriculus and intestines were clearly filled and the lumen clearly outlined with contrast. All images represent time points where contrast material was visible within the cloaca, though the actual minutes varied. Visualization scores were significantly lower in the midazolam-butorphanol (MD) group (median score 0, range 0–1) and in the midazolam (M) group (median score 1, range 0–1) than in the control group (median score 2, range 1–2).

creased gastric and intestinal emptying times.[25] The effect of butorphanol was dose-dependent with higher doses of butorphanol having a more suppressive effect on GI transit time.[25] In horses, xylazine (0.5 mg/kg) and butorphanol (0.05 mg/kg) given in combination have profound suppressive effects on equine duodenal motility.[14] Butorphanol (0.05 mg/kg) also decreased gastric emptying in ponies.[11] In people, opioids delay gastric emptying.[15,21,22,24,27] It is assumed that this effect is mediated by peripheral μ-opioid receptors highly concentrated in the gastric antrum and proximal duodenum.[15] In ventilated, critically-ill human patients, midazolam-morphine caused a significant delay in gastric emptying time compared to propofol.[23]

Midazolam at 6 mg/kg had a less clinically significant effects on GI transit times compared to the MB protocol. In mice, comparatively higher dosages of midazolam (25 and 50 mg/kg) delay GI transit and gastric emptying in a dose-dependent manner.[13] In contrast, in people, a low dose of midazolam at 0.03 mg/kg followed by a second dose at 0.015 mg/kg increased duodenal motility but did not affect retroperistalsis.[28] In another study, diazepam increased the gastric emptying rate and overall motility in people.[20] In cats, ketamine (13.2 mg/kg) and diazepam (0.44 mg/kg) had minimal effects on GI transit time, while ketamine alone increased gastric contractions and decreased GI transit time.[12] The benzodiazepine-mediated effects on GI transit times and motility are possibly dose-dependent. Dose-dependent effects of midazolam and butorphanol were not evaluated in this study. The delaying effect of butorphanol and midazolam (given in combina-

Table 1. Time (min) to presence of contrast media in different gastrointestinal (GI) segments in 12 cockatiels (6 females [F]; 6 males [M]) after gavage administration of iohexol (20 mL/kg) into the crop. Birds were randomly assigned to 3 treatment groups of midazolam (6 mg/kg IM), midazolam-butorphanol (3 mg/kg + 3 mg/kg IM), and a control group to assess the effects of sedation on GI transit times; sedative drugs were administered 15 minutes before iohexol administration.

	Proventriculus			Ventriculus			Intestines			Cloaca		
Bird	C	M	MB	C	M	MB	C	M	MB	C	M	MB
F1	5	5	15	15	5	15	15	15	30	60	60	120
F2	5	5	5	5	5	5	15	15	30	120	120	120
F3	5	5	15	5	5	30	5	5	60	30	30	120
F4	5	5	5	5	5	5	5	5	30	60	120	180
F5	5	5	5	5	15	60	5	15	60	60	120	180
F6	5	5	5	5	15	15	5	15	30	30	60	120
M7	5	5	5	5	5	30	5	5	30	60	60	120
M8	5	5	120	5	5	120	15	15	120	60	60	180
M9	5	15	60	15	15	60	15	30	120	60	120	180
M10	5	5	5	5	5	5	5	5	15	30	60	120
M11	5	5	5	5	5	15	5	5	15	120	120	120
M12	5	5	5	5	5	5	5	5	30	120	120	180
Median	**5**	**5**	**5**	**5**	**5**	**15**[a,b]	**5**	**10**	**30**[a,b]	**60**	**90**[a]	**120**[a,b]
Min	5	5	5	5	5	5	5	5	15	30	30	120
Max	5	15	120	15	15	120	15	30	120	120	120	180

Abbreviations: C indicates control group; M, midazolam; MB, midazolam-butorphanol.
[a] $P < .05$ compared to control group.
[b] $P < .05$ compared to midazolam group.

Table 2. Esophageal bolus and ventricular contraction frequency in 12 cockatiels (6 females [F]; 6 males [M]) after gavage administration of iohexol (20 mL/kg) into the crop. Birds were randomly assigned to 3 treatment groups of midazolam (6 mg/kg IM), midazolam-butorphanol (3 mg/kg + 3 mg/kg IM), and a control group to assess the effects of sedation on these parameters; sedative drugs were administered 15 minutes before iohexol administration.

	Esophageal bolus frequency per minute						Ventricular contractions per minute					
	30 minutes			60 minutes			30 minutes			60 minutes		
Bird	C	M	MB	C	M	MB	C	M	MB	C	M	MB
F1	8	11	3	11	8	3	3	1	0	3	2	0
F2	7	11	0	7	9	0	8	0	0	4	0	0
F3	12	14	2	18	13	5	11	1	0	11	4	0
F4	12	4	10	13	12	8	12	n/a	1	0	0	0
F5	11	4	0	8	11	4	7	3	0	5	3	0
F6	11	12	16	16	11	16	5	0	0	6	0	3
M7	15	13	15	15	15	12	9	n/a	0	4	0	1
M8	3	6	1	13	14	1	7	3	n/a	5	3	0
M9	2	12	0	6	16	11	8	2	0	6	3	0
M10	n/a	10	10	1	15	8	7	0	0	6	2	0
M11	10	4	0	12	8	0	8	1	0	8	0	0
M12	10	7	13	13	5	11	8	0	0	6	0	0
Mean	**9.2**	**9.0**	**5.8**	**11.1**	**11.4**	**6.6**[a,b]	**7.8**	**1.1**[a]	**0.1**[a,b]	**5.3**	**1.4**[a]	**0.3**[a,b]
SD	3.9	3.8	6.4	4.8	3.4	5.2	2.4	1.2	0.3	2.7	1.6	0.9
Min	2	4	0	1	5	0	3	0	0	0	0	0
Max	15	14	16	18	16	16	12	3	1	11	4	3

Abbreviations: C indicates control group; M, midazolam; MB, midazolam-butorphanol; n/a, not available.
[a] $P < .05$ compared to control group.
[b] $P < .05$ compared to midazolam group.

tion) on GI transit times possibly is a dose-dependent phenomenon. Because butorphanol and midazolam are currently 2 of the most commonly used analgesic and sedative drugs in psittacine birds, effects on GI transit time should be considered when using these drugs to provide analgesia and sedation in birds.

Doses of midazolam were chosen based on literature describing a midazolam dose of 7.5 mg/kg as a sole agent in Indian ring-necked parakeets (*Psittacula krameri*).[29] Butorphanol doses have been reported up to 5 mg/kg in Hispaniolan Amazon parrots (*Amazona ventralis*).[30] Thus, a 6 mg/kg dose of midazolam as a sole agent and a combination dose of 3 mg/kg midazolam and 3 mg/kg butorphanol were considered reasonable for the size of bird in our study.

Performing GI contrast studies in sedated birds has not been recommended because of the reduced intestinal function secondary to these drugs.[3] Our results confirmed that sedative drugs can have an effect on GI transit time and motility. However, our results also showed that GI contrast studies can be performed safely in sedated birds and that the use of midazolam does not have clinically significant effects, with the exception of overall transit time and ventricular contraction frequency. Therefore, GI contrast studies performed under sedation will produce the same diagnostic results as in unsedated birds if GI obstruction, luminal distension (eg, proventricular dilatation), or intracoelomic nongastroinstestinal mass effects (eg, organomegaly or neoplasia) are to be investigated. The results of GI contrast studies in sedated birds should not be compared to results obtained in unsedated birds, because certain GI transit parameters as well as motility can be affected by the use of sedative drugs. Hence, hypo- or hypermotility of the GI tract cannot be reliably diagnosed in sedated birds unless specific reference values have been established for specific sedation protocols in different avian species.

Historically, barium has been more commonly reported and used clinically over iohexol as an oral contrast agent in birds.[31,32] However, iohexol may be safer when the risk of aspiration is high. Unlike barium, iohexol did not induce any histologic changes in rat lung tissues.[33] Barium used for bronchography has been demonstrated to cause mild intra-alveolar granulomatous pneumonia that did not cause any clinical signs in horses.[34] It has been suggested that aspiration of barium in birds results in less severe clinical signs compared to mammals because of differences in lower respiratory tract anatomy and the lack of blind-ending alveoli.[3] Barium also is contraindicated when there is risk of a gastrointestinal perforation.[3] In our study, iohexol was used instead of barium because of the reduced risks if regurgitation should occur and the faster GI transit times of iohexol compared to barium.[2,3] Because faster GI transit time and a subsequently shorter time to obtain results is preferable in most cases, iohexol should be considered instead of barium, in particular if avian patients are sedated. Barium has been recommended over the use of organic iodine compound contrast media (eg, iohexol), because of the apparent poorer image quality.[3] However, iohexol provides adequate contrast for GI imaging in psittacine birds compared to barium and it provided good visualization of the entire GI tract in the cockatiels in our study.[2] Doses recommended for iohexol and other, nonionic iodinated contrast agents vary from 10 to 30 mL/kg.[2,3] Preliminary fluoroscopic studies were performed with 5, 10, and 20 mL/kg iohexol (unpublished data) in cockatiels. At doses of 5 and 10 mL/kg, radiographic contrast was not adequate to assess ventricular contractions and esophageal boluses. Because the 20 mL/kg dose was well tolerated in preliminary trials, this dose of iohexol was chosen to use in the study.

The images were scored for visualization or intensity of contrast by a blinded observer. In all sedated birds, visualization was graded significantly poorer than in control birds. The score was lower in the MB than in M groups. A possible reason for this finding is that decreased motility may have resulted in decreased transit of contrast material into the ventriculus and intestines. This reduced amount of contrast within the ventriculus and intestines may have been diluted with intestinal contents, resulting in reduced visualization scores.

The length of the fasting period and time of day can affect GI transit times.[3,35–37] Birds in this study were fasted for 1 hour, and all experiments were performed during the same hours of the day. Therefore, these factors should have had a limited effect on our results. Habituation to the imaging enclosure also may have affected our results. However, randomization of the treatment sequence was used to mitigate this effect.

This study investigated the effects of midazolam and midazolam-butorphanol on GI transit times and motility in cockatiels. Midazolam-butorphanol and midazolam sedation protocols had clinically and statistically significant effects on GI transit time and ventricular contractions. The effects of midazolam-butorphanol were more

pronounced than with midazolam alone. Esophageal contractions were not affected by midazolam, but were affected by midazolam-butorphanol. Clinicians should carefully consider the drugs used for sedation and their effects on GI transit times and motility when performing GI contrast studies in psittacine birds.

References

1. McMillan MC. Imaging techniques. In: Ritchie BW, Harrison GJ, Harrison LR, eds. *Avian Medicine, Principles and Application*. Lake Worth, FL: Wingers Publishing Inc; 1994:256–259.
2. Ernst S, Goggin JM, Biller DS, et al. Comparison of iohexol and barium sulfate as gastrointestinal contrast media in mid-sized psittacine birds. *J Avian Med Surg*. 1998;12(1):16–20.
3. Krautwald-Junghanns M-E, Schroff S, Bartels T. Birds. In: Krautwald-Junghanns M, Pees M, Reese S, Tully TN, eds. *Diagnostic Imaging of Exotic Pets: Vögel-Kleinsäuger-Reptilien*. Hannover, Germany: Schlütersche; 2011:1–142.
4. Kubiak M, Forbes NA. Fluoroscopic evaluation of gastrointestinal transit time in African grey parrots. *Vet Rec*. 2012;171(22):563.
5. Beaufrère H, Nevarez J, Taylor WM, et al. Fluoroscopic study of the normal gastrointestinal motility and measurements in the Hispaniolan Amazon parrot (*Amazona ventralis*). *Vet Radiol Ultrasound*. 2010;51(4):441–446.
6. Vink-Nooteboom M, Lumeij JT, Wolvekamp WT. Radiography and image-intensified fluoroscopy of barium passage through the gastrointestinal tract in six healthy Amazon parrots (*Amazona aestiva*). *Vet Radiol Ultrasound*. 2003;44(1):43–48.
7. Denbow DM. Gastrointestinal anatomy and physiology. In: Scanes CG, ed. *Sturkie's Avian Physiology*. 6th ed. St Louis, MO: Elsevier; 2014:337–366.
8. Mans C, Guzman DS, Lahner LL, et al. Sedation and physiologic response to manual restraint after intranasal administration of midazolam in Hispaniolan Amazon parrots (*Amazona ventralis*). *J Avian Med Surg*. 2012;26(3):130–139.
9. Doss GA, Mans C. Changes in physiologic parameters and effects of hooding in red-tailed hawks (*Buteo jamaicensis*) during manual restraint. *J Avian Med Surg*. 2016;30(2):127–132.
10. Mans C. Sedation of pet birds. *J Exotic Pet Med*. 2014;23(2):152–157.
11. Doherty TJ, Andrews FM, Provenza MK, Frazier DL. The effect of sedation on gastric emptying of a liquid marker in ponies. *Vet Surg*. 1999;28(5):375–379.
12. Hogan PM, Aronson E. Effect of sedation on transit time of feline gastrointestinal contrast studies. *Vet Radiol*. 1988;29(2):85–88.
13. Inada T, Asai T, Yamada M, Shingu K. Propofol and midazolam inhibit gastric emptying and gastrointestinal transit in mice. *Anesth Analg*. 2004;99(4):1102–1106.
14. Merritt AM, Burrow JA, Hartless CS. Effect of xylazine, detomidine, and a combination of xylazine and butorphanol on equine duodenal motility. *Am J Vet Res*. 1998;59(5):619–623.
15. Murphy DB, Sutton JA, Prescott LF, Murphy MB. Opioid-induced delay in gastric emptying: a peripheral mechanism in humans. *Anesthesiology*. 1997;87(4):765–770.
16. Roebel LE, Cavanagh RL, Buyniski JP. Comparative gastrointestinal and biliary tract effects of morphine and butorphanol (Stadol). *J Med*. 1979;10(4):225–238.
17. Steyn PF, Twedt D, Toombs W. The effect of intravenous diazepam on solid phase gastric emptying in normal cats. *Vet Radiol Ultrasound*. 1996;38(6):469–473.
18. Sutton DGM, Preston T, Christley RM, et al. The effects of xylazine, detomidine, acepromazine and butorphanol on equine solid phase gastric emptying rate. *Equine Vet J*. 2002;34(5):486–492.
19. Topcu I, Ekici NZ, Isik R, et al. The effects of dexmedetomidine and midazolam on gastrointestinal motility in septic rats. *Anesth Analg*. 2006;102(3):876–881.
20. Schurizek BA, Kraglund K, Andreasen F, et al. Gastrointestinal motility and gastric pH and emptying following ingestion of diazepam. *Br J Anaesthes*. 1988;61(6):712–719.
21. Mittal RK, Frank EB, Lange RC, McCallum RW. Effects of morphine and naloxone on esophageal motility and gastric emptying in man. *Dig Dis Sci*. 1986;31(9):936–942.
22. Nimmo WS, Heading RC, Wilson J, et al. Inhibition of gastric emptying and drug absorption by narcotic analgesics. *Br J Clin Pharmacol*. 1975;2(6):509–513.
23. Nguyen NQ, Chapman MJ, Fraser RJ, et al. The effects of sedation on gastric emptying and intragastric meal distribution in critical illness. *Intensive Care Med*. 2008;34(3):454–460.
24. Crighton IM, Martin PH, Hobbs GJ, et al. A comparison of the effects of intravenous tramadol, codeine, and morphine on gastric emptying in human volunteers. *Anesth Analg*. 1998;87(2):445–449.
25. Scrivani PV, Bednarski R, Myer C. Effects of acepromazine and butorphanol on positive-contrast upper gastrointestinal tract examination in dogs. *Am J Vet Res*. 1998;59(10):1227–1233.
26. Doss GA, Williams JM, Mans C. Determination of gastrointestinal transit times in barred owls (*Strix varia*) by contrast fluoroscopy. *J Avian Med Surg*. 2017;31(2):123–127.
27. Yuan CS, Foss JF, O'Connor M, et al. Effects of low-dose morphine on gastric emptying in healthy volunteers. *J Clin Pharmacol*. 1998;38(11):1017–1020.

28. Castedal M, Björnsson E, Abrahamsson H. Effects of midazolam on small bowel motility in humans. *Aliment Pharmacol Ther*. 2000;14(5):571–577.
29. Vesal N, Eskandari MH. Sedative effects of midazolam and xylazine with or without ketamine and detomidine alone following intranasal administration in ring-necked parakeets. *J Am Vet Med Assoc*. 2006;228(3):383–388.
30. Guzman DS, Flammer K, Paul-Murphy JR, et al. Pharmacokinetics of butorphanol after intravenous, intramuscular, and oral administration in Hispaniolan Amazon parrots (*Amazona ventralis*). *J Avian Med Surg*. 2011;25(3):185–191.
31. Krautwald-Junghanns M-E, Schloemer J, Pees M. Iodine-based contrast media in avian medicine. *J Exotic Pet Med*. 2008;17(3):189–197.
32. Wagner WM, Kirberger RM. Radiographic gastrointestinal contrast study in the ostrich (*Struthio camelus*). *Vet Radiol Ultrasound*. 2003;44(5):546–552.
33. Ginai AZ, ten Kate FJ, ten Berg RG, et al. Experimental evaluation of various available contrast agents for use in upper gastrointestinal tract in case of suspected leakage. Effects on lungs. *Br J Radiol*. 1984;57(682):895–901.
34. Walker M, Goble D. Barium sulfate bronchography in horses. *Vet Radiol*. 1980;21(2):85–90.
35. Duke GE, Evanson OA. Diurnal cycles of gastric motility in normal and fasted turkeys. *Poult Sci*. 1976;55(5):1802–1807.
36. Duke GE, Dziuk HE, Hawkins L. Gastrointestinal transit-times in normal and bluecomb diseased turkeys. *Poult Sci*. 1969;48(3):835–842.
37. Buyse J, Adelsohn DS, Decuypere E, Scanes CG. Diurnal, nocturnal changes in food intake, gut storage of ingesta, food transit time and metabolism in growing broiler chickens: a model for temporal control of energy balance. *Br Poult Sci*. 1993;34(4):699–709.