Butorphanol-Midazolam Combination Injection for Sedation of Great White Pelicans *(Pelecanus onocrotalus)*

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ABSTRACT

Successful conscious sedation in wildlife veterinary medicine contributes significantly to the efficient and effective care of avian patients, provided in a safe environment for wildlife handlers. Great White Pelicans (*Pelecanus onocrotalus*) on bi-annual migrations between Europe and Africa commonly arrive at the Israeli Wildlife Hospital (IWH) for treatment for various injuries sustained en route. Due to their aggressive nature, the staff at the IWH evaluated the efficacy of a combination of butorphanol and midazolam (BM) on sedation, measured via physiologic (body temperature, heart rate, and respiratory rate) and behavioral (aggressiveness, neck posture, and eye closure) parameters on 7 adult/sub-adult Great White Pelicans: 3 males, weight 9.40 ± 1.14 kg (mean ± standard deviation) and 4 females, weight 6.65 ± 0.87 kg. Effects of BM sedation (1mg/kg midazolam, 0.5mg/kg butorphanol, IM) on the various parameters were recorded at 10, 15, and 30 minutes (min) and 1, 2, 3, 4, and 5 hours (h) after injection. As early as 10 min after injection of BM, 43% of the birds were less aggressive and 29% exhibited a flaccid neck posture and closed eyes. The maximum response for eye closure (86%) occurred at 30 min and that for both neck posture and aggression (100% for both) at 15 min. The only physiologic parameter to display a statistically significant decrease after sedation was heart rate ($p < 0.001$), though an absence of an increase in other physiologic parameters suggests a tolerance for human-induced stress. Normal behavioral and physiologic parameters of the pelicans were recovered after 5 h from the initial sedation without any apparent clinical side effects. These results show that contrary to the high dosages of butorphanol published in the literature, a combination of butorphanol and midazolam can be administered at significantly lower dosages with satisfactory sedation in Great White Pelicans.

Keywords: Butorphanol, Midazolam, Conscious sedation, Great White Pelican, *Pelecanus onocrotalus*.

INTRODUCTION

Abiding by its mission to treat injured wild animals and release them back to nature, the Israeli Wildlife Hospital (IWH) treats an average of 50 injured Great White Pelicans (*Pelecanus onocrotalus*) annually. Pelicans often stop to feed and rest in Israel during their biannual spring and autumn migrations between Europe and Africa. Approximately 70,000 pelicans pass over Israel during the autumn migration period (1) and some sustain injuries including, but not limited to, the results of illegal hunting, collisions with power lines, and entanglement with fishing nets (personal information).

The total length of the Great White Pelican ranges from 140 to 175 cm, of which the large bill accounts for 28 to 39 cm (2). The average adult male weighs between 9 and 15 kg, with the smaller female averaging 5.4 to 9 kg (3). Demonstrated by their girth, pelicans are large birds whose

aggressive characteristics make it difficult to handle them during physical examinations, radiography, ultrasonography and/or venipuncture, and require more than one person to safely restrain and treat these birds.

Animal hospitals utilize both butorphanol and midazolam in avian veterinary practice (4) for various purposes. Butorphanol is a synthetic, centrally-acting, narcotic agonist-antagonist analgesic with potent antitussive activity, commonly administered for both acute and chronic pain management. Midazolam, a benzodiazepine tranquilizer, is a drug used for treating acute seizures and moderate to severe insomnia, and for inducing sedation when combined with an analgesic before medical procedures (5). Though the combination of butorphanol and midazolam (BM) is not routinely used to induce conscious sedation in avian patients during basic clinical procedures, it does, however, offer several significant advantages for intensive treatment, such as the reduction of stress elicited by manual restraint and stress-induced hyperthermia and tachypnea (6-9). The following research suggests that the use of a BM combination will both reduce the stress of the treated animals and further ensure the safety of animal handlers.

MATERIALS AND METHODS

Birds

This study was conducted on 7 adult and sub-adult Great White Pelicans (*Pelecanus onocrotalus*), comprised of 4 females weighing 6.65 ± 0.87 kg (mean ± standard deviation) and 3 males weighing 9.40 ± 1.14 kg, with an overall range of 5.8–10.2 kg. They were submitted to the IWH for various reasons, including, but not limited to gun-shot wounds, exhaustion, and orthopedic injuries from collisions. After confirmation of adequate health based on physical examination, radiology, and blood tests, the pelicans underwent rehabilitation as a condition for release. The rehabilitation period ensures that the pelicans held for treatment at the IWH are able to be released with full capability to compete and migrate in their natural populations. This study was performed during this pre-release rehabilitation period. The pelicans were successfully released to nature upon completion of their treatment course.

Sedation process

During the rehabilitation period, all 7 birds received an intramuscular saline injection equal to the amount in milliliters of BM calculated for each individual animal as a control for physiological and behavioral parameters susceptible to intramuscular injections. Three days post control, all 7 pelicans received an injection of midazolam (Midazolam 5 mg/ml, dosage 1mg/kg IM; Rafa Laboratories Ltd., Jerusalem, Israel) and butorphanol (Torbugesic 10 mg/ml, dosage 0.5mg/kg IM; Fort Dodge Animal Health, Fort Dodge, IO, USA) combined in one syringe.

Monitoring of physiological and behavioral parameters

The pelicans were monitored before and after administration of sedation agents for several physiological and behavioral parameters. The physiological parameters that were measured were body temperature, heart rate, and respiratory rate; the behavioral parameters included neck posture, eye closure, and aggressiveness.

Control measurements for the saline injections were taken immediately before the injection and at 10 and 15 min after injection. Experimental measurements were taken immediately before injection of the BM combination, and at 10, 15, and 30 min, and 1, 2, 3, 4, and 5 h after injection.

The physiological parameters were measured as follows: body temperature was measured in the cloaca with a digital thermometer (Vega Technologies Inc. Taiwan) (Figure 1), heart rate was measured with a stethoscope (Classic 2 SE; Littmann, USA), and respiratory rate was counted by the examining technician or veterinarian.

Behavioral parameters that were considered a response to sedation ("abnormal") were considered to be folded or leaning necks (Figure 2 a, b), closed or semi-closed eyes, and an absence of response to humans. Normal behavioral parameters were described as a straight neck, open eyes, and normal aggressive behavior (Figure 3), demonstrated by biting, attempting to escape, and vocalization. All measurements were taken by the same person and all procedures and behavioral parameters were documented by video camera for further confirmation of the sedation response.

Statistical methods

In order to determine the effects of sedation and time on these parameters, one-way analysis of variance (ANOVA)

Figure 1: A physical examination by a veterinarian shows the cloacal temperature measurement on a sedated pelican. The butorphanol and midazolam combination sedation technique allows for restraint-free handling of birds that typically display aggressive behavior towards animal caretakers.

Figure 3: An unsedated pelican displays a normal aggressive behavior towards an animal caretaker. Other aggressive behaviors include charging, biting, escaping, and loud vocalizations.

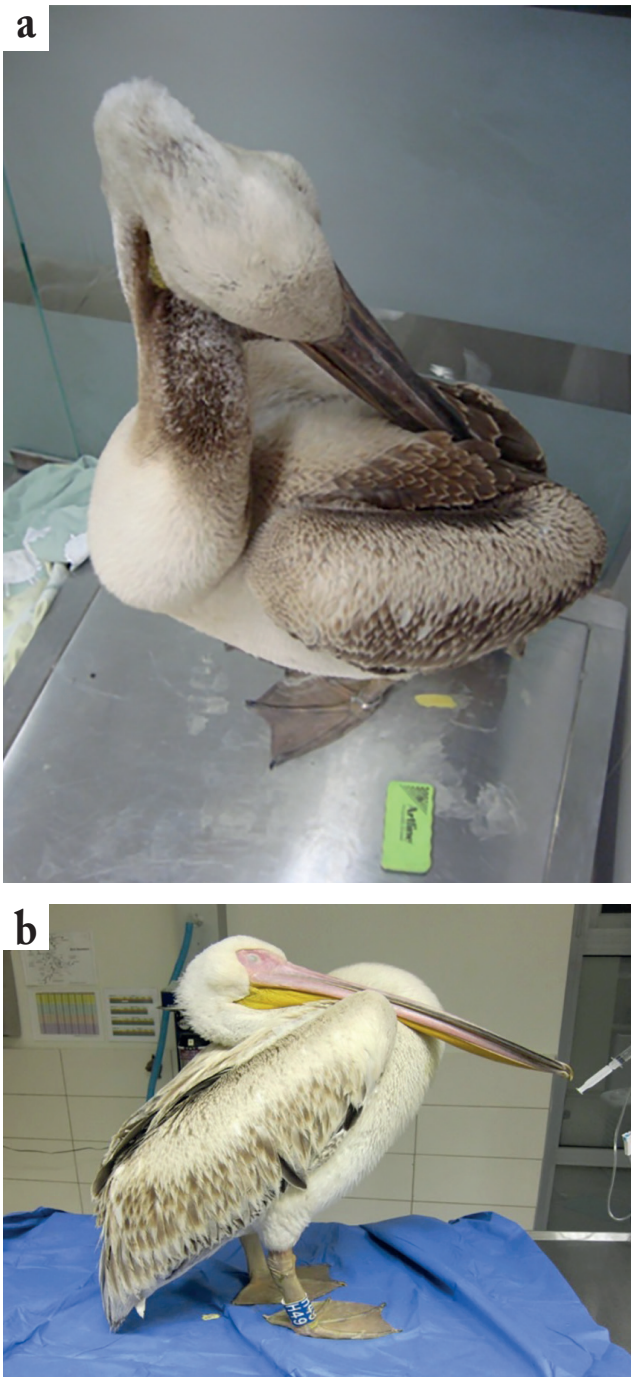

Figure 2: Fifteen minutes after a combined butorphanol and midazolam sedation injection, normally aggressive pelicans display the behavioral parameters of (a, b) folded necks and (b) closed eyes, indicative of a successful sedation for veterinary assessment.

and Duncan's multiple-range-test were applied by means of the SAS/STAT software. Groups were considered significantly different with a p-value less than 0.05. The proportions of birds with normal and abnormal ratings of the behavioral parameters (head posture, opening of eyes, and aggression) before and following sedation, respectively, were analyzed for significance by application of the chi-square test with the SAS/STAT software.

RESULTS AND DISCUSSION

Several physiological and behavioral parameters were monitored in 7 Great White Pelicans that were admitted for clinical evaluation and treatment at the IWH. All were tested for conscious sedation efficacy under both saline and BM injection and behavioral and physiologic observations were recorded for up to 15 minutes and 5 hours post-injection, respectively.

Table 1 presents the values (mean ± standard deviation) of body temperature, heart rate, and respiratory rate, starting before sedation and up to 5 h post-sedation.

The results of the statistical analysis of the data in Table 1 are presented in Table 2, which indicates heart rate as the only physiological parameter that showed a statistically significant decrease post-sedation at every time point (p<0.001). Although an increased respiratory rate is expected in the control group due to human-induced stress, the data did not show a statistically significant decrease in respiratory rate post-sedation (p = 0.06). Although the physiologic param-

Table 1: Average levels (mean ± standard deviation) of body temperature, heart rate and respiratory rate pre-sedation and up to 5 h post-sedation.

Time	Body Temperature ˚C	Heart rate beats/min	Respiratory rate breaths/min
Pre-sedation			
0 min	40.3 ± 0.53	214 ± 42	9 ± 2.6
10 min	ND	196 ± 50	7 ± 2.6
15 min	40.0 ± 0.53	175 ± 45	9 ± 2.6
Post-sedation			
0 min	±40.4 0.53	197 ± 40	8 ± 2.6
10 min	ND	129 ± 34	5 ± 2.6
15 min	39.9 ± 0.53	114 ± 29	7 ± 2.6
30 min	39.9 ± 0.26	103 ± 24	7 ± 2.6
1 hrs	39.6 ± 0.79	109 ± 26	6 ± 2.6
2 hrs	39.7 ± 0.79	99 ± 26	6 ± 2.6
3 hrs	39.6 ± 0.53	103 ± 24	6 ± 2.6
4 hrs	40.0 ± 0.26	111 ± 32	7 ± 2.6
5 hrs	39.6 ± 0.45	110 ± 18	5 ± 2.2

ND = Not determined.

Table 2: One-way analysis of variance of effects of sedation, time during sedation, and the interaction of sedation and time, of the three physiological parameters: body temperature, heart rate, and respiratory rate.

Independent variables	Dependent variables	Body Temp ˚C	Heart rate beats/min	Respiratory rate breaths/min
Sedation		NS	p < 0.001	NS
Time (of sedation)		NS	p < 0.001[1]	NS
Sedation × Time		NS	NS	NS

NS = Not significant, p > 0.05
[1] time 0 > all time points, p < 0.01

Table 3: Numbers of pelicans with normal or abnormal presentation of three behavioral parameters – neck posture, eye closure, and aggression – pre-sedation and up to 5 h post-sedation and the significance of the differences (p-values) between the proportions.

Time	Neck posture[1]			Eyes[2]			Aggression[3]		
	Normal	Abnormal (% of sample)	p	Normal	Abnormal (% of sample)	p	Normal	Abnormal (% of sample)	p
Pre-sedation	7	0 (0)	0.001	7	0 (0)	0.001	7	0	0.001
Post-sedation									
0 min	7	0 (0)	0.001	7	0 (0)	0.001	7	0 (0)	0.001
10 min	5	2 (29)	NS	5	2 (29)	NS	4	3 (43)	NS
15 min	0	7 (100)	0.001	2	5 (71)	NS	0	7 (100)	0.001
30 min	0	7 (100)	0.001	1	6 (86)	0.01	0	7 (100)	0.001
1 hrs	0	7 (100)	0.001	2	5 (71)	NS	0	7 (100)	0.001
2 hrs	0	7 (100)	0.001	4	3 (43)	NS	0	7 (100)	0.001
3 hrs	1	6 (86)	0.01	4	3(43)	NS	1	6 (86)	0.01
4 hrs	2	5 (71)	NS	5	2 (29)	NS	1	6 (86)	0.01
5 hrs	1	4 (80)	NS	4	1 (20)	NS	1	4 (80)	NS

NS = Not statisically significant (p > 0.05)
[1] Normal = straight Abnormal = folded, leaning
[2] Normal = open Abnormal = closed or semi-closed
[3] Normal = biting/escaping Abnormal = no response

eters did not decrease as expected, the absence of an increase in these parameters should be noted. A constant respiratory rate and internal temperature provides evidence that additional stress was not induced with the BM treatment. The data did not show any combined effects of sedation and duration of sedation on these parameters (sedation × time).

Table 3 presents the number of birds displaying normal and sedative manifestations for the three behavioral parameters – head posture, eye closure, and aggression – pre- and post-sedation and the statistical significance of the differences between the control and experimental injections. All 7 subjects displayed the sedative presentations of head posture and aggression at 15 min post-sedation (p = 0.001 for both behaviors); eye closure occurred at 30 min post sedation (p = 0.01)

Previous research by Figueiredo *et al.* (10), Lennox (11), and Mans *et al.* (12) presented the administration of a high dosage of butorphanol (1-3 mg/kg) and a low dosage of midazolam (0.25-1 mg/kg) as effective sedation agents in avian veterinary medicine. However, contrary to the high dosages of butorphanol previously published in established literature, the results presented here confirm that a combination of butorphanol and midazolam can be administered at significantly lower dosages (0.5 mg/kg butorphanol, 1 mg/kg midazolam) with satisfactory sedation in Great White Pelicans. Only 10 to 15 min after BM injection, the behavioral parameters of the test subjects suggested significant decrease in stress levels, allowing for easy manual restraint by only one technician while carrying out physical examinations, radiography, ultrasonography and/or venipuncture. Supported by the static physiologic parameters post-sedation, the behavioral changes in Great White Pelicans treated with a low dose BM combination confirms an absence of additional human-induced stress associated with animal treatment and can furthermore provide adequate protection to those involved with the care of Great White Pelicans.

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