Effect of Alfaxolone in Raptors: Pilot Study in Common Kestrels (Falco tinnunculus)

JL. Mendoza, DVM; I. López, DVM; S. Casado, BS; V. Valenzuela, DVM; J. Benito, DVM, MS; O. Martín-Jurado, DVM; F. González, DVM

GREFA Wildlife Hospital and Rehabilitation Center
C/ Monte del Pilar, s/n. 28220. Majadahonda, Madrid (Spain)
e-mail: *fgonzalez@grefa.org*

MADRID 2011
11th European AAV Conference
1st ECZM Meeting

Abstract

Alfaxalone has been re-formulated and currently there are very few studies in avian species using this new formulation. The aim of this pilot study is to describe cardiorespiratory effects and the degree of sedation of alfaxalone administered intramuscularly in common kestrels (*Falco tinnunculus*).

Adult male and female common kestrels hospitalized and considered non-releasable were anaesthetized with alfaxolone (Alfaxan®) using 2.5, 5, 10 and 20 mg/kg administered intramuscularly. Heart and respiratory rate, non-invasive arterial blood pressure and temperature were monitored. Time from drug administration until the first signs of ataxia and total sedation time were noted. Degree of sedation and quality of recovery were assessed using different scales.

There were no complications from anaesthesia and recovery. First signs of sedation (ataxia) appeared within 2 min of administration. Degree of sedation and duration of anaesthesia (from 10 to 35 min) was dose dependent. Cardiorespiratory depression was observed with all doses and was dose dependent.

Previous studies in dogs and cats suggested minimal cardiorespiratory depression. Alfaxolone produced dose dependent cardiorespiratory depression and sedation in common kestrels.

Introduction and Objetive

Alfaxalone is a steroid anaesthetic agent, highly water-insoluble and historically was formulated in combination with alphadololone and Cremophor-EL, a solubilizing agent (Zaki et al. 2009). However, in humans, dogs and cats, hypersensitivity reactions related to the diluent Cremophor-EL led the withdrawal of Althesin® (Glaxo) and Saffan® (Shering Plough Animal Health) (Muir et al. 2008; Prys-Roberts and Sear, 1975).

The CT1341 and later Saffan® were popularized as an anaesthetic for use in birds in the 70's (Cooper and Frank, 1973 and 1974). Fatal complications and electrocardiographic changes with alfaxolone were previously described in birds (Cooper and Redig, 1975; Frank and Cooper, 1976; Cribb and Haigh, 1977), but this anaesthetic was used successfully in the 80´s. Alfaxalone has been re-formulated (Figure 1) and marketed in Europe in 2009 (Alafaxan®, Vetoquinol) in combination with 2-hydroxypropil-beta-cyclodextrin (HPCD) increasing the solubility and making possible to reduce intramuscular doses in birds. However, little information in avian species reporting this new formulation is available and the suitable intramuscular doses are sparse.

The aim of this clinical pilot study is to explore and describe cardiorespiratory effects and the degree of sedation of clinical doses of a new formulation of alfaxalone to better define a suitable intramuscular dose in common kestrels (*Falco tinnunculus*).

Figure 1.

Material and Methods

After obtaining the approval of the Institutional Animal Care and Use Committee (GREFA IACUC, Wildlife Hospital and Rehabilitation Center, Majadahonda-Madrid, Spain), two adult male and four female common kestrels (Falco tinnunculus), all of them being admitted in GREFA (Wildlife Hospital and Rehabilitation Center, Majadahonda-Madrid, Spain) and considered non-releasable, were anaesthetized with alfaxolone (Alfaxan®) using 2.5, 5, 10 and 20 mg/kg administered intramuscularly. Clinical doses administered in this study were selected from the clinical dose range reported previously in birds (Samour et al. 1984; Harcourt-Brown, 1978) and from the sparse information provided by Vetoquinol.

Heart and respiratory rate, temperature and non-invasive arterial blood pressure were monitored (Figure 2). Time from drug administration until the first signs of ataxia and total sedation time were noted. Degree of sedation and quality of recovery were assessed using different scales. Tracheal intubation was attempted to evaluate the response to the stimulus.

This pilot study was conducted as a crossover randomized by dose. Each animal was anesthetized four times. Four intramuscular doses (2.5, 5, 10 and 20 mg/kg) were administered in random order. Each dose was separated by at least one-week washout period.

Numerical variables were analyzed using analysis of variance. A one-way analysis of variance (ANOVA) for repeated measures (dose x time) was performed with the intra-subject factor being the time and the inter-subject factor being the drug. The Bonferroni test was employed to compare dose-groups. A p value of <0.05 was set to indicate statistical significance. Categorical data were analyzed using nonparametric procedures. All analyses and graphs were performed using the GraphPad Prism 4 (GrapghPad Software, Inc. USA).

Table 1.

Animals	ID	Gender	# Anesthesia	2.5 mg/kg	5 mg/kg	10 mk/kg	20 mg/kg
1	W0792	Female	4	✓	✓	✓	✓
2	W0752	Female	4	✓	✓	✓	✓
3	W0626	Female	3		✓	✓	✓
4	W0728	Female	4	✓	✓	✓	✓
5	W0577	Male	4	✓	✓	✓	✓
6	W0725	Male	3	✓	✓	✓	

Table 2.

		2.5 mg/kg	5 mg/kg	10 mg/kg	20 mg/kg
Total Animals (n)		5	6	6	5
	Male	2	2	2	1
	Female	3	4	4	4
Weight *Mean (SD)*		190 (27.8)	192.7(27.8)	194.7 (25.2)	196.4 (23.4)
	Male	163 (12.7)	185 (9.9)	172 (0.0)	194 (0.0)
	Female	208 (15.9)	196.5 (22.4)	206 (23.4)	197 (20.5)
General Status (1-5) *Mean (SD)*		2 (0.7)	2 (0.6)	1.5 (0.5)	1.8 (1.0)
	Male	2.5 (0.7)	1.5 (0.7)	2 (0.0)	1.0 (1.0)
	Female	1.7 (0.6)	2.3 (0.5)	1.3 (0.5)	2.0 (0.8)

Results

Four kestrels were anesthetized four times with the described doses. Two kestrels were only anesthetized 3 times at different doses (Table 1). A total number of 22 anaesthetic procedures were performed (Table 2). Most anaesthetic procedures did not show any complications during anaesthetic maintenance and recovery. However, unfortunately two kestrels could not complete the four doses scheduled. One of the female kestrels (W0626) died after being anaesthetized without any problem at 10 mg/kg during recovery. Necropsy of this animal could not explain this fatal complication. One male kestrel was euthanized because of the worsening of its injuries and the appearance of pain. Minor complications recorded in this pilot study were excitement and variable level of sedation. First signs of sedation (ataxia) after administration of 2.5, 5, 10 and 20 mg/kg appeared within 4.18 ± 4.2, 3.04 ± 3.00, 4.06 ± 7.70 and 1.19 ± 1.3 min of drug administration respectively (Table 3). Degree of sedation and duration of anaesthesia was dose dependent; 2.5 and 5 mg/kg produced very light sedation over 5 minutes. The administration of 10 mg/kg produced mild sedation within 4.50 ± 7.90 min over a period of 23.61 ± 5.1 min. The administration of 20 mg/kg produced moderate sedation within 2.20 ± 2.7 min over a period of 49.61 ± 12.5 min (Figure 6). Cardiorespiratory depression was observed with all doses but not significantly differences were observed between dosages (Figure 4-5). Non-invasive arterial blood pressure could not be monitored accurately because an inappropriate level of anaesthesia at 2.5, 5 and 10 mg/kg doses. Significant changes in temperature were not observed (Figure 7). Tracheal intubation was only successful when 20 mg/kg dose was administered (Table 4).

Time	min, mean (SD)	2.5 mg/kg	5 mg/kg	10 mk/kg	20 mg/kg
0	Time of IM administration of Alfaxan	-	-	-	-
1	Time of ΔHR				
.					
.	Time of loss of head hanging down	4.18 (4.2)	3.04 (3.00)	4.50 (7.90)	2.20 (2.7)
4	Time of loss of standing position	9.40(9.4)	4.90(6.80)	4.26(7.50)	2.02(3.1)
5	Time to achieve/gaining standing position	12.50 (12.5)	9.23(11.60)	27.87 (33.70)	51.63 (65.4)
6	Time of total recovery and release to the cage	12.35 (13.8)	12.44 (16.50)	32.90 (35.40)	54.88 (69.3)

Table 3.

Table 4.

Group	#Intubated Animals	Animal ID	Gender	T0	T5	T10	T15	T20	T25	T30	T35
2.5 mg/kg n=5	n= 0	1 W0725	M	N	N	N					N
		2 W0792	F	N							
		3 W0728	F	N							
		4 W0577	M	N	N	N					
		5 W0752	F	N	N						
5 mg/kg n=6	n= 0	6 W0626	F	N	N	N					N
		3 W0728	F	N	N	N					N
		1 W0725	M	N	N						
		2 W0792	F	N							
		4 W0577	M	N	N	N					
		5 W0752	F	N	N	N					
10 mg/kg n=6	n= 2	2 W0792	F	N	N	Y					N
		1 W0725	M	N	N	N					N
		6 W0626	F	N	N	N					N
		3 W0728	F	N	N	N					N
		4 W0577	M	N	N	N					N
		5 W0752	F	Y	N	N					N
20 mg/kg n=5	n= 3	3 W0728	F	N	Y	N					N
		6 W0626	F	N	N	N					N
		2 W0792	F	N	N	Y					Y
		4 W0577	M	Y	N	N					N
		5 W0752	F	N	N	N					N

Figure 2.

Figure 3.

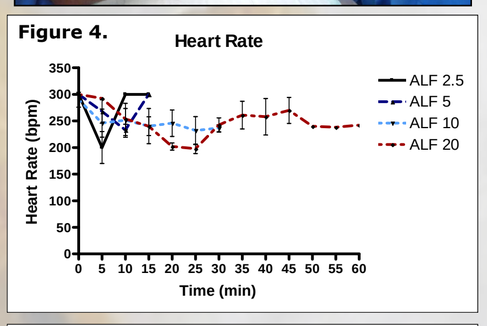

Figure 4.

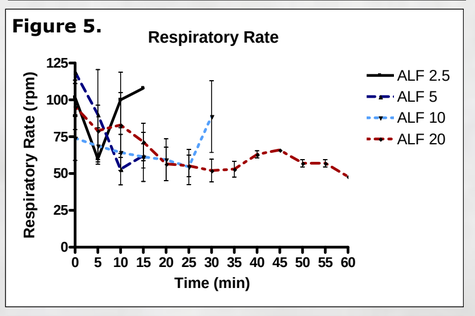

Figure 5.

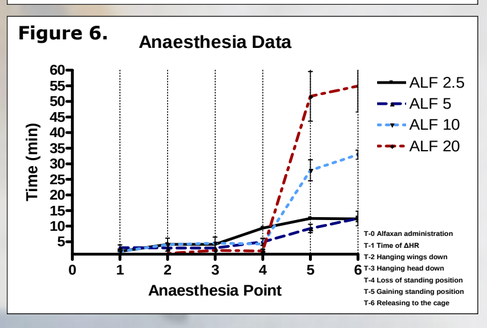

Figure 6.

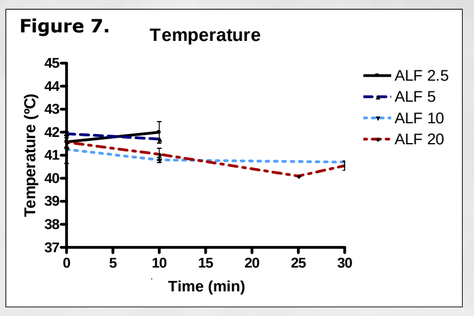

Figure 7.

Discussion and Conclusions

In this pilot study Alfaxalone (Alfaxan®, Vetoquinol) did not produce adequate level of anesthesia and sedation when 2.5 and 5 mg/kg doses were administered. Short length of action was found at 10 mg/kg. However, short diagnostic procedures could be performed at doses 10 and 20 mg/kg. Recovery period was short at each dose and was accompanied mostly by excitement. Alfaxolone (Alfaxan®, Vetoquinol) produced dose dependent cardiorespiratory depression and sedation in common kestrels. Intubation was not easily performed, being only successful when the highest dose was administered.

Alfaxalone has been used in avian practice for over 40 years, but there are few published doses rates for individual species (Samour et al. 1984; Bailey et al. 1999). Previous anaesthetic procedures in common kestrels were reported (Harcourt-Brown, 1978) at doses ranging 34-38 mg/kg. The large volume required for intramuscular administration with previous formulations made the new formulation with higher solubility, a tentative new-old good anaesthetic drug of choice.

Further studies comparing different combinations with other sedatives and anaesthetic drugs regarding these same doses and route of administration used in this pilot-study are guaranteed. Combinations of alfaxalone have been previously reported in avian practice (Harcourt-Brown, 1978; Gandini et al. 1986; Cullen et al. 1995).

In conclusion, alfaxalone (Alfaxan®) produced dose dependent cardiorespiratory depression and sedation in common kestrels, but only short not-painful procedures at doses of 10 and 20 mg/kg administered intramuscularly could be performed.

Citation Index

1. BALEY TA, TOOSI A, SAMOUR JH. Anaesthesia of cranes with alphaxolone-alphadolone.*Vet Rec. 1999 Jul 17;145(3):84-5.* 2. CRIBB AND HAING. Anaesthetic for avian species. *Veterinary Record 100: 472-473. 1977* 3. COOPER AND FRANK. Use of the steroid anaesthetic CT1341 in birds. *Veterinary Record 92, 474. 1973*. 4. COOPER JE AND FRANK LG. The use of the steroid anaesthetic CT 1341 in birds. *Raptor Research 8 :20. 1974.* 5. COOPER AND REDIG P. *Veterinary Record 97. 352. 1975* 6. CULLEN LK, GOERKE MA, SWAN RA, CLARK WT, NANDAPI D, COLBOURNE C. Ostrich anaesthesia: xylazine premedication followed by alphaxalone/alphadolone and isoflurane. *Aust Vet J. 1995 Apr;72(4):153-4.* 7. FRANK LG, COOPER JE. *Raptor Research 8:29. 1976.* 8. GANDINI GC, KEFFEN RH, BORROUGHS RE, EBEDES H.. An anaesthetic combination of ketamine, xylazine and alphaxalone-alphadolone in ostriches (Struthio camelus). *Vet Rec. 1986 Jun 28;118(26):729-30.* 9. MUIR W, LERCHE P, WIESE A, NELSON L, PASLOSKE K, WHITTEM T. Cardiorespiratory and anesthetic effects of clinical and supraclinical doses of alfaxalone in dogs. *Vet Anaesth Analg. 35(6):451-462. 2008.* 10. PRYS-ROBERTS C, SEAR J. Steroid anaesthesia. *Br J Anaesth. 52(4):363-365. 1980*. 11. SAMOUR JH, JONES DM, KNIGHT JA, HOWLETT JC. Comparative studies of the use of some injectable anaesthetic agents in birds. *Vet Rec.115(1):6-11. 1984*. 12. ZAKI S, TICEHURST K, MIYAKI Y. Clinical evaluation of Alfaxan-CD(R) as an intravenous anaesthetic in young cats. *Aust Vet J. 87(3): 82-87. 2009.*

Acknowledgements

The willingness of the Márcia Bettencourt Viana and Virginia Moraleda Fernández (Avutardos Study Group) to participate in this pilot-study is truly appreciated. We would like to thank them for their help with the discussion of this poster. We would like to thank Dr Mila Freire (Comparative Pain Research Laboratory, NCSU) for her help with the final designed poster.