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Effective Field Immobilization of Andean Fox (*Lycalopex culpaeus*) with Ketamine-Dexmedetomidine and Antagonism with Atipamezole

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ABSTRACT: A combination (mean±SD) of ketamine (4.0±1.0 mg/kg in juveniles and 3.0±0.4 in adults) and dexmedetomidine (0.055±0.01 and 0.049±0.01, respectively), reversed with atipamezole (at 10 mg/mg of dexmedetomidine), was assessed in 57 Andean foxes (*Lycalopex culpaeus*) in field conditions. Induction times in juveniles and adults were 4.6±3.9 min and 4.3±2.4 min, respectively. Immobilization was smooth and safe, and lasted 50±8 min in juveniles and 50±10 min in adults. Full recovery was recorded at 40±29 min in juveniles and 37±23 min in adults after atipamezole administration. Drug dose, season, body temperature, and fox sex and body condition were not related to variations in induction and recovery times, body temperature, heart rate, respiratory rate, or hemoglobin oxygen saturation. No side effects were observed other than a slight but significant decrease in mean body temperature during the procedure. This combination allowed carrying out all the typical procedures of a research project, including the collection of several biologic samples.

Key words: Anesthesia, atipamezole, Canidae, chemical immobilization, culpeo fox, dexmedetomidine, ketamine, *Pseudalopex culpaeus*.

Immobilization for noninvasive procedures is commonly utilized for the safety of investigators and animals (Chinnadurai et al. 2016). The Andean (culpeo) fox (*Lycalopex culpaeus*) is widespread in South America (Lucherini 2016). A study including 28 South American grey foxes (*Lycalopex griseus*) and five Andean foxes compared three immobilization protocols: ketamine and medetomidine, ketamine and xylazine, or tiletamine-zolazepam (Acosta-Jamett et al. 2010). However, mixing species and the low number of individuals tested per protocol hindered the interpretation of the results. Dexmedetomidine is the pharmacologically active form of the two optical enantiomers that comprise the α2-agonist medetomidine, with a greater selectivity for the α2-receptor than the racemate (Murrell and Hellebrekers 2005). Dexmedetomidine may have greater clinical benefits compared to medetomidine (Ansah et al. 1998). For example, better cardiovascular stability has been observed in rabbits (*Oryctolagus cuniculus*; Lima et al. 2014), and better quality in the anesthesia and deeper analgesia was observed in golden-headed lion tamarins (*Leontopithecus chrysomelas*; Selmi et al. 2004). So far, the only evaluation of the use of ketamine-dexmedetomidine in a wild canid was in 16 African wolves (*Canis lupaster*; Gutema et al. 2018). This combination was also used, but not evaluated, in a study including 15 Sechuran foxes (*Lycalopex sechurae*; Lescano et al. 2018). This combination and ketamine-midazolam was also compared in oncilla (*Leopardus tigrinus*; Da Lima et al. 2016). The aim of our study was to assess a ketamine-dexmedetomidine combination and its reversal with atipamezole in a representative sample of field-trapped Andean foxes.

During an epidemiologic study, 57 foxes (four juvenile males, 11 juvenile females, 23 adult males, and 19 adult females) were captured in central Chile with leg-hold traps (Soft Catch no. 1.5, Oneida Victor Inc., Euclid, Ohio, USA). Traps were checked at dawn and captured foxes were restrained with a pole, transferred to a restraining cage, weighed using a Pesola scale (Pesola AG, Baar, Switzerland) to the nearest 0.1 kg, and injected intramuscularly with the ketamine-dexmedetomidine combination. During the first captures we adjusted the dose based on the observed times until we obtained a smooth immobilization during the time necessary to carry out all study procedures. This resulted in

TABLE 1. Results of immobilization of 57 Andean foxes (*Lycalopex culpaeus*) with ketamine-medetomidine reversed with atipamezole. SpO_2 = hemoglobin oxygen saturation.

Measurement (unit)	Juveniles			Adults		
	n	Mean	SD	*n*	Mean	SD
Body condition (scale: 1–5)	15	2.1	0.4	42	2.5	0.6
Ketamine[a]* (mg/kg)	15	4.01	1.02	42	3.04	0.39
Dexmedetomidine[b]* (mg/kg)	15	0.055	0.007	42	0.049	0.006
Atipamezole[c]* (mg/kg)	15	0.56	0.07	42	0.49	0.05
Induction time (min)	15	4.6	3.9	42	4.3	2.4
Total immobilization time[d] (min)	14	50.5	8.1	42	50.1	10.5
Time to first signs of recovery[e] (min)	13	4.1	6.8	42	3.9	3.7
On-feet time[e] (min)	14	11.5	16.3	42	10.3	6.1
Time to full recovery[e] (min)	11	40.5	29.6	41	36.9	23.2
Body temperature (C)	15	38.1	1.2	42	38.2	1.0
Body temperature, variation (C)	15	−0.66	0.07	42	−0.78	0.47
Heart rate (beats/min)	14	77.7	26.6	42	77.9	17.6
Hear rate, variation (beats/min)	14	−6.4	19.2	42	+0.91	17.2
Respiratory rate (breaths/min)	14	21.7	3.6	42	20.3	4.4
Respiratory rate, variation* (breaths/min)	14	+0.85	3.6	42	−2.1	3.5
SpO_2 (%)	12	92.6	5.3	34	91.5	3.9
SpO_2, variation (%)	8	−0.50	7.3	32	−0.12	25.3

[a] Dexdomitor©, Zoetis, Santiago, Chile.
[b] Ketostop©, Drag Pharma, Santiago, Chile.
[c] Antisedan©, Zoetis.
[d] From ketamine-dexmedetomidine administration to atipamezole administration.
[e] After atipamezole administration.
* Statistically significant differences between juveniles and adults.

juveniles receiving a significantly higher mean dose than did adults (Mann-Whitney *U*-test, $z=3.1$, $P<0.001$ for ketamine; $z=2.4$, $P<0.05$ for dexmedetomidine and atipamezole; Table 1). Therefore, juveniles received a mean (±SD) dose of 4.0±1.0 mg/kg of ketamine plus 0.055±0.007 mg/kg of dexmedetomidine whereas adults received 3.0±0.4 mg/kg plus 0.049±0.006 mg/kg, respectively. No such differences occurred between sexes.

Monitoring of immobilization included, every 10 min, recording body temperature (BT; measure in the rectum, C), using a digital thermometer; heart rate (HR, beats/min) using a stethoscope; hemoglobin oxygen saturation (SpO_2, percent) using a peripheral pulse oximeter (CMS60D-VET, Contec Co., Qinhuangdao, China); respiratory rate (RR, breaths/min, visually); and presence of palpebral and anal reflexes. We monitored time to induction (time between first injection and when the fox was fully immobilized); time from reversal (i.e., atipamezole administration) to first signs of recovery and arousal (usually head movements); on-feet time after reversal (first attempts at walking); and time from reversal to full recovery. A subjective body condition score ranging from 1 (emaciation) to 5 (obese) was given to each fox by one observer (A.C.). Any physical reactions to the drug combination were noted (e.g., vomiting, excessive salivation, compulsive licking, muscle twitching). When possible, ambient temperature during the procedure was recorded (range 5–25 C). Immobilized foxes were wrapped in a blanket to maintain BT; a hot water bottle was placed under the animals during the colder months. Necessary supplies and equipment were available in case of emergency (Chinnadurai et al. 2016). After the procedures were finished (weight and measures recording, blood extraction, ecto-

parasites, hair, and swabs collection, microchip implantation), the fox was transferred to a cage and 10 mg of atipamezole per milligram of dexmedetomidine was administered intramuscularly (Table 1). The cage was covered with a blanket and placed in a quiet place. One of the team members stayed close to the cage and observed the fox every minute. The fox was released at the capture point after full recovery.

Univariate general linear models, including only adult foxes, were used to evaluate the potential effects of sex and body condition, season and ambient temperature, and ketamine and dexmedetomidine doses on: induction time, BT, RR, HR, and SpO_2 and their variations between the beginning and end of the procedure. A multivariate analysis of variance with the three recovery times (time to first recovery signs, on-feet time, and total recovery time) as dependent variables was used to evaluate the effects of sex and body condition, season and ambient temperature, ketamine and dexmedetomidine doses, and atipamezole dose and immobilization duration in recovery times. Binary logistic regression models were used to evaluate the association between the probability of a fox reacting to blood extraction and the need for ketamine supplementation, with sex and body condition and with ketamine and dexmedetomidine doses. A backward stepwise elimination method was used in which the least significant variable ($P<0.1$) was removed after each step. Differences in immobilization times, BT, HR, RR, and SpO_2, and their variations between the beginning and end of the procedure were compared between age groups using a Mann-Whitney *U*-test. Kruskal-Wallis analysis was used to compare the evolution of BT, HR, RR, and SpO_2 over time. Continuous variables that were not normally distributed were log-transformed. Analyses were performed with PASW Statistics 19 (SPSS Inc., Chicago, Illinois, USA).

Induction time was about 4 min in both adults and juveniles. Immobilizations lasted 50 min and were generally smooth, safe, and allowed carrying out of all the procedures. No adverse physical reactions were observed. Ten individuals (three juveniles and seven adults) needed a second dose of ketamine consisting of half the original dose. Five foxes started to move their heads by the end of the procedure; in these cases, atipamezole was applied immediately. All animals maintained the palpebral reflex during the procedure. Full recovery after atipamezole injection lasted 37 min in adults and 40 min in juveniles (Table 1).

None of the studied factors was related to the immobilization and recovery times. Mean BT in adults was 38 C, with a slight but constant mean decrease during the procedure (Kruskal-Wallis, $\chi^2=20.1$, $P<0.001$; Fig. 1), which was independent of the ambient temperature. Only two foxes reached 40 C at some point of the procedure. Mean HR, RR, and SpO_2 were similar between age groups. Models indicated that mean HR was higher in females (82.6±18.3 beats/min) than in males (72.1±15.2 beats/min; $F=4.7$, $P<0.05$) whereas the opposite was observed for SpO_2 (90.0±4.2% vs. 93.4±2.4%; $F=5.5$, $P<0.05$). Significant variations in RR between age groups were found: RR increased during the procedure in juveniles and decreased in adults ($z=2.6$, $P<0.01$; Table 1).

We used a higher dose of dexmedetomidine and lower dose of ketamine than did Gutema et al. (2018) because ketamine cannot be reversed, but immobilization times (induction, arousal, and on-feet times), HR, and RR were similar in both studies. Compared to the medetomidine-ketamine combination used in one Andean fox and 10 South American grey foxes by Acosta-Jamett et al. (2010), induction times were similar, but the time to first signs of recovery was shorter in our study (4 min vs. 7 min). Unfortunately, Acosta-Jamett et al. (2010) did not report full recovery times. We recorded smaller HR (77 vs. 87 beats/min) and RR (21 vs. 32 beats/min) than did their study and similar SpO_2. Both studies observed the presence of palpebral reflexes in all the animals. Compared to the medetomidine-ketamine combination used with 32 red foxes (*Vulpes vulpes*) by Shilo et al. (2010) in Israel, we observed shorter induction but prolonged on-feet times; HR and RR were markedly

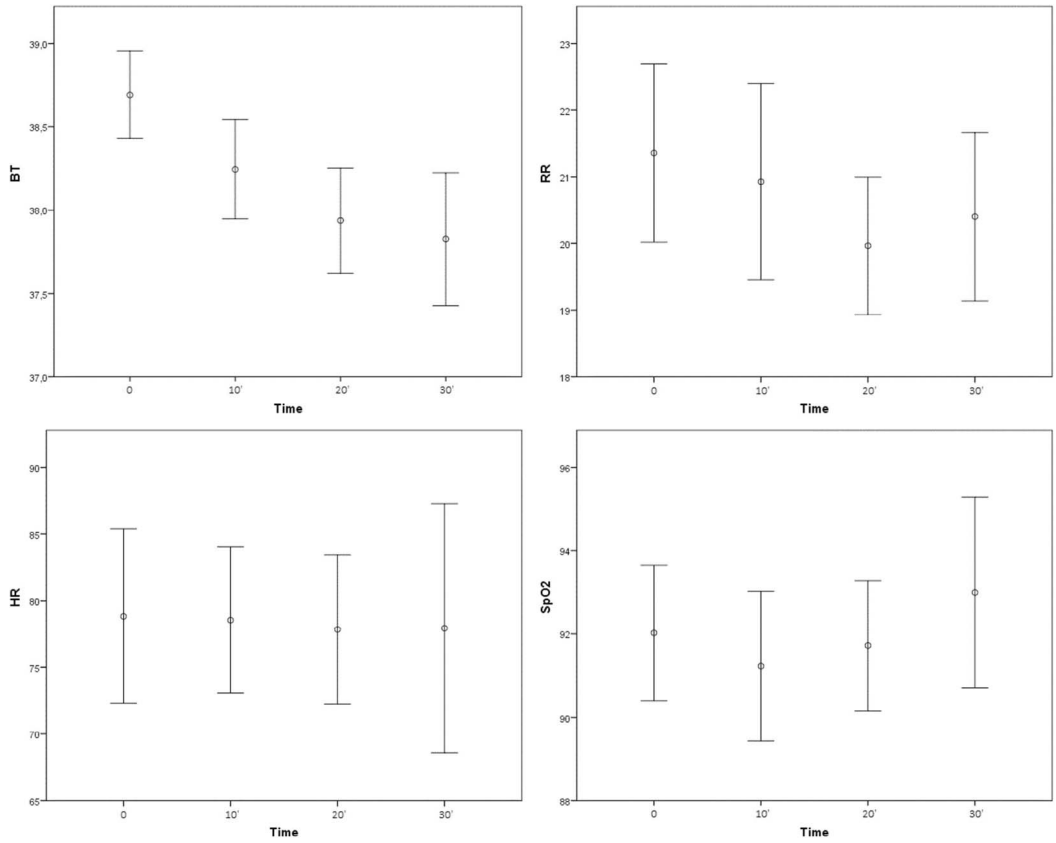

FIGURE 1. Variation in mean body temperature (BT), respiratory rate (RR), heart rate (HR), and hemoglobin oxygen saturation (SpO_2) every 10 min during immobilization using a combination of ketamine-dexmedetomidine in 42 adult Andean foxes (*Lycalopex culpaeus*). Data expressed as mean and SD.

lower in our study and BT and SpO_2 were in the same range.

Although the HR we measured were lower than in studies using ketamine-medetomidine in other studies on foxes, we did not notice signs of cardiovascular depression, as we did not detect any significant variation in HR and RR during the procedures. However, in contrast to Gutema et al. (2018), who reported hyperthermia as a side effect of this protocol in Ethiopian wolves (*Canis simensis*), a decrease in mean BT was observed during our procedures. This decrease might have been higher if we had not applied heat to some foxes when the environmental temperature was low. Hypothermia has been reported as a potential side effect of the use of dexmedetomidine in dogs (Granholm et al. 2007). This adverse effect should be taken into account by researchers and veterinarians when using the protocol that we studied, especially during cold conditions.

In conclusion, we recommend the combination of ketamine-dexmedetomidine in Andean foxes and other South American foxes. Lower doses of ketamine should be evaluated to obtain shorter full recovery times.

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