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## Ketamine and Midazolam Anesthesia in Pacific Martens (*Martes caurina*)

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**ABSTRACT:** The use of midazolam as a tranquilizer for anesthesia in mustelids in conjunction with the cyclohexamine ketamine is not well documented. Because midazolam is fast acting, inexpensive, and quickly metabolized, it may serve as a good alternative to other more commonly used tranquilizers. We trapped and anesthetized 27 Pacific martens (*Martes caurina*) in Lassen National Forest (northern California, US) August 2010–April 2013. We assessed anesthesia with ketamine at 18 and 25 mg/kg combined with 0.2 mg/kg of midazolam by comparing mean times of induction, return to consciousness, and recovery, plus physiologic parameters. No reversal was used for the midazolam portion of the anesthetic. Mean ( $\pm$ SD) induction for both ketamine dosages was  $1.7\pm 0.5$  and  $1.8\pm 1.0$  min, respectively. Return to consciousness mean times were 8.0 min longer ( $P<0.001$ ) for martens receiving a 25 mg/kg ketamine dosage. Mean recoveries were 15.1 min longer ( $P<0.003$ ) for the 25 mg/kg ketamine dosage. Physiologic parameter means were similar for both ketamine dosages with no statistically significant differences. Body temperatures and heart and respiratory rates were generally stable, but percentage of oxygen saturation and end tidal carbon dioxide values were below those seen in previous mustelid studies. The combination of ketamine, at both dosages, and midazolam provided reliable field anesthesia for Pacific martens, and supplemental oxygen is recommended as needed.

**Key words:** American marten, anesthesia, ketamine, *Martes americana*, *Martes caurina*, midazolam, Pacific marten.

Field studies documenting anesthesia protocols for the genera *Martes* and *Pekania* (martens and fishers) have focused on the use of cyclohexamines combined with  $\alpha_2$ -adrenergic tranquilizers (Belant 2005; Belant 2007), and the inhalation gas, isoflurane (Desmarchelier et al. 2007). Gas anesthesia results in short induction and recovery times, plus stable physiologic parameters; however, equip-

ment expense, portability, reliability in lower temperatures, and training are obstacles for routine use during field efforts (Kocer and Powell 2009). Therefore, injectable anesthetic agents are typically used in field situations despite decreased anesthetic control.

Negative effects have been noted with the use of  $\alpha_2$ -adrenergic tranquilizers in mustelids, including bradycardia, apnea, and decreased body temperature (Fournier-Chambrillon et al. 2003). Midazolam, a benzodiazepine tranquilizer, combined with the cyclohexamine, ketamine, may be useful as an alternative. Midazolam is fast acting, inexpensive, injected intramuscularly, and quickly metabolized—all beneficial qualities for field use. Further, benzodiazepines have muscle relaxant and anticonvulsant properties, potentially counteracting an increased likelihood of seizures by mustelids anesthetized with ketamine (Plumb 2011). The use of midazolam has not been reported for North American Martens (*Martes americana* and *Martes caurina*), but has been in river otters (*Lontra canadensis*) (Kimber et al. 2000) and fishers (*Pekania pennanti*) (Bunting et al. 2010). Typically, midazolam's reversal agent flumazenil has not been used because of partial results and high cost (Plumb 2011).

Several dosage references suggest anesthetic drug combinations for martens (Kollias and Abou-Madi 2007; Kreeger and Arnemo 2012), but none specifically for ketamine and midazolam. We selected a base dosage of 18 mg/kg ketamine and a second higher dosage for comparison to achieve longer handling times. The higher dosage was determined using metabolic scaling (Kreeger 1996) but would have

been nearly a 100% increase above the base. Instead, we used a more conservative increase of approximately 50%. Midazolam was used at 0.2 mg/kg for all captures (Stepien et al. 2000). We compared induction, recovery times, and physiologic parameters of Pacific Martens (*M. caurina*) anesthetized intramuscularly with 18 versus 25 mg/kg ketamine hydrochloride (Ketaset<sup>®</sup>, 100 mg/mL, Fort Dodge Animal Health, Fort Dodge, Iowa, USA), combined with 0.2 mg/kg midazolam hydrochloride (Versed<sup>®</sup>, 5 mg/mL, Bedford Laboratories, Bedford, Ohio, USA).

Martens were handled for a habitat study between August 2010 and April 2013 in Lassen National Forest, northern California (40°30'N, 121°7'W). We used box-traps (model 108, Tomahawk Live Trap Company, Tomahawk, Wisconsin, USA) with corrugated plastic sheeting added to the bottom of each trap to minimize potential claw damage and to sanitize between captures. Wooden boxes were attached to the back of each trap to provide additional shelter. Traps were checked daily and baited with chicken and an olfactory lure (Gusto, Minnesota Trapline Products, Pennock, Minnesota, USA). As needed, traps were covered with tree boughs and bark to minimize the captured martens' exposure to inclement weather.

Anesthesia was induced by moving each marten from the wooden box through a cloth handling funnel attached to a metal cone and injected intramuscularly (Hearn 2007). Martens are sexually dimorphic; doses for each gender were based on average weights (mean  $\pm$  SD; female 648  $\pm$  93 g, male 1,026  $\pm$  100 g) of previously captured martens during our study. Because of the small volumes needed, both anesthetic drugs were placed in a single vial and withdrawn using a 1.0 mL syringe for administration. Some of the adult martens (>2 yr) previously captured needed global positioning system (GPS) radio collars, which required two captures

10–30 days apart. These martens were given a randomly assigned (18 or 25 mg/kg) first dosage of ketamine and the other dosage was used when removing the collar.

Anesthetic times quantified included induction, defined as the time from drug injection to no response to noxious stimuli (anesthesia depth stage 3) using the Guedel (1951) classification; return to consciousness, defined as the end of induction to when the marten was able to again respond to stimuli (anesthetic depth stage 2); and recovery, defined as the end of induction to when the marten was able to stand with controlled, purposeful movement. After initial physical examinations, anesthetic monitoring was conducted at 5-min intervals postinduction and included anesthetic depth, heart rate (HR), respiratory rate (RR), rectal temperature (T), oxyhemoglobin saturation percentage (SpO<sub>2</sub>), and end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>). Heart rate and SpO<sub>2</sub> were measured using a portable pulse oximeter (Smiths Medical Inc, SurgiVet V3402, Waukesha, Wisconsin, USA) with the sensor placed on the tongue. Rectal T was determined using a digital thermometer. The RR and ETCO<sub>2</sub> were determined using a portable capnograph (Oridion Microcap Plus, Jerusalem, Israel) with an infant-sized sensor at the nostril and nasal passages.

Statistical analyses were performed with SAS software (SAS Institute Inc., Cary, North Carolina, USA). Anesthesia times and physiologic parameters were compared using two-tailed Student's *t*-tests of the initial captures (Bonferroni correction factor for multiple comparisons), and means are reported with standard deviations. Factors of age, gender, month of capture, and ambient temperature were analyzed by comparing their means and standard deviations for both ketamine dosages. Anesthesia data from martens captured twice for GPS collar placement and removal using both ketamine dosages were assessed for intermarten variability

TABLE 1. Anesthesia time in minutes (mean±SD) for Pacific Martens (*Martes caurina*) following intramuscular injection of ketamine at two dosages (18 and 25 mg/kg) and midazolam (0.2 mg/kg).

Period	18 mg/kg (n=12)	25 mg/kg (n=15)
Induction	1.7±0.5	1.8±1.0
Return to consciousness <sup>a</sup>	16.8±5.0	24.8±5.3
Recovery <sup>a</sup>	40.3±8.4	55.4±13.6

<sup>a</sup> Statistically different (corrected  $P \leq 0.03$ ).

using the same statistical methods described earlier. Capture methods were approved by Oregon State University's Animal Care and Use Committee (Permits: 3944, 4367) and the California Department of Fish and Wildlife Memorandum of Understanding with a Scientific Collecting permit (Permit: 803099-01).

We anesthetized 27 martens (eight females, 19 males), each induced with a single intramuscular injection and having a complete set of anesthetic monitoring data postinduction. There was no difference in mean inductions between ketamine dosage groups of 18 and 25 mg/kg, most likely reflecting rapid absorption of ketamine and midazolam (Plumb 2011). Martens given 25 mg/kg ketamine had significantly longer return to consciousness mean times (anesthetic depth 2) with difference of 8.0 min (df=26;  $P < 0.001$ ; Table 1). Recoveries for the 25 mg/kg group were also longer, with a mean difference of 15.1 min (df=26;  $P < 0.003$ ). Physiologic parameter means were similar for both ketamine dosages with no statistically significant differences (Table 2). Body T, HR, and RR were generally stable for the three monitored times. However, SpO<sub>2</sub> and ETCO<sub>2</sub> values were below those seen in previous mustelid studies. Values for age, gender, month of capture, and ambient temperature had similar means and overlapping standard deviations for both ketamine dosages. Because of this, no further statistical testing methods were conducted.

For martens anesthetized twice (four females, nine males), mean induction

TABLE 2. Anesthetic monitoring parameters (mean±SD) for times 5, 10, 15 min postinduction for Pacific Martens (*Martes caurina*) anesthetized intramuscularly with ketamine at two dosages (18 and 25 mg/kg) and midazolam at 0.2 mg/kg.

Parameters	18 mg/kg (n=12)	25 mg/kg (n=15)
Temperature (C)		
5	39.0±0.9	38.8±1.0
10	38.6±0.9	37.9±0.8
15	38.1±0.8	37.3±1.0
Heart rate (beats/min)		
5	287±74	279±73
10	269±45	277±54
15	287±20	304±35
Respiration rate (breaths/min)		
5	41±21	42±16
10	40±10	48±18
15	40±15	38±26
Oxyhemoglobin saturation %		
5	64.7±10.2	65.7±8.2
10	76.4±8.2	72.6±10.3
15	79.0±5.6	63.0±4.8
End tidal CO <sub>2</sub>		
5	26.8±10.7	26.5±7.8
10	31.4±11.2	27.3±8.8
15	30.5±7.7	32.5±21.5

times were similar for both ketamine dosages, 1.6±0.6 and 1.6±0.7 min (df=25;  $P=0.85$ ), respectively. Mean times for return to consciousness and recovery were greater with the higher ketamine dosage, a difference of 13.2 min (df=25,  $P=0.0003$ ) and 15.8 min (df=25,  $P=0.0001$ ), respectively. Physiologic parameters were not significantly different.

Both dosage levels (18 and 25 mg/kg) of ketamine combined with 0.2 mg/kg midazolam given intramuscularly induced repeatable, predictable unconsciousness assessed to be light to moderate stage 3 anesthesia (Guedel 1951). Inductions were quick (1–3 min) for both ketamine dosages, whereas return to consciousness and recoveries were extended by approximately 8 and 15 min, respectively. This time extension was valuable for providing safe handling and data collection. Recoveries for both ketamine dosages occurred

on average in less than 1 h from induction. In comparison, recoveries for inhalant anesthesia were shorter for (Desmarchelier et al. 2007) but longer and with more variation for reported injectable anesthetic studies in martens (Belant 1992; Belant 2005).

Physiologic parameters were consistent between both dosages of ketamine and comparable with previous research. Throughout anesthetic monitoring, body temperatures remained within 37.5–38.9 C, which were similar to findings of Desmarchelier et al. (2007) and Belant (2005). Desmarchelier et al. (2007) recorded a mean  $\text{ETCO}_2$  of 40.4, compared with the average values (26–32) of this study. Mean  $\text{ETCO}_2$  levels were low but could be explained by rapid respiration rates or shallow positioning of the nares capnograph tube. Respiratory rates were consistent to previous studies using injectable anesthetic agents (Belant 2007) and isoflurane (Desmarchelier et al. 2007). The  $\text{SpO}_2$  means recorded in this study were much lower than expected given observed RRs and mucus membrane color with physical examinations. The pulse oximeter sensor clip was frequently checked for accuracy, and no known underlying physiologic pathology in the martens was determined. A more likely explanation for low  $\text{SpO}_2$  values relates to the size of the sensor clip used, which was calibrated for the tongues and ears of dogs and cats. Measurements from the thinner marten tongue allowed for correct pulse monitoring of arterial blood, but likely registered falsely low  $\text{SpO}_2$  values because of minimal tissue absorbance of light (i.e., penumbra effect; Dugdale 2010). An upward trend in  $\text{SpO}_2$  was noted during anesthetic monitoring intervals, but only for the 18 mg/kg ketamine dosage. Given the low  $\text{SpO}_2$  values we observed, we recommend using supplemental oxygen with this anesthetic drug combination, unless pulse oximetry with a smaller clip proves this unnecessary. Cardiovascular stability is common with ketamine-in-

duced anesthesia. Mean HRs in our study were greater than previously recorded means for both injectable and inhalant anesthetics (Desmarchelier et al. 2007). Between-marten variability of anesthesia effects of this drug combination appears low, but our sample size limited a more rigorous assessment using generalized linear mixed models. In conclusion, the combination of ketamine, at both dosages, and midazolam provided reliable field anesthesia for Pacific Martens with supplemental oxygen recommended as needed. Increasing the ketamine dosage to 25 from 18 mg/kg provided an average of 8 min additional handling time.

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