DOI: 10.7589/2011-12-366 Journal of Wildlife Diseases, 49(2), 2013, pp. 403–407

Evaluation of Medetomidine-Ketamine and Atipamezole for Reversible Anesthesia of Free-ranging Gray Wolves (*Canis lupus*)

Jon M. Arnemo,[1,2,3,6] Alina L. Evans,[1,3] Per Ahlqvist,[4] Peter Segerström,[5] and Olof Liberg[4] [1]Department of Forestry and Wildlife Management, Faculty of Applied Ecology and Agricultural Sciences, Hedmark University College, Campus Evenstad, NO-2418 Elverum, Norway; [2]Department of Wildlife, Fish and Environmental Studies, Faculty of Forest Sciences, Swedish University of Agricultural Sciences, SE-90183, Umeå, Sweden; [3]Section of Arctic Veterinary Medicine, Department of Food Safety and Infection Biology, Norwegian School of Veterinary Science, Stakkevollveien 23, NO-9010 Tromsø, Norway; [4]Grimsö Wildlife Research Station, Department of Conservation Biology, Faculty of Natural Resources and Agricultural Sciences, Swedish University of Agricultural Sciences, SE-73091 Riddarhyttan, Sweden; [5]Vaikijaur 617, SE-96299 Jokkmokk, Sweden; [6]Corresponding author (email: jon.arnemo@hihm.no)

ABSTRACT: Twenty-eight anesthetic events were carried out on 24 free-ranging Scandinavian gray wolves (*Canis lupus*) by darting from a helicopter with 5 mg medetomidine and 250 mg ketamine during winter in 2002 and 2003. Mean±SD doses were 0.162±0.008 mg medetomidine/kg and 8.1±0.4 mg ketamine/kg in juveniles (7–10 mo old) and 0.110±0.014 mg medetomidine/kg and 5.7±0.5 mg ketamine/kg in adults (>19 mo old). Mean±SD induction time was shorter ($P<0.01$) in juveniles (2.3±0.8 min) than in adults (4.1±0.6 min). In 26 cases, the animals were completely immobilized after one dart. Muscle relaxation was good, palpebral reflexes were present, and there were no reactions to handling or minor painful stimuli. Mild to severe hyperthermia was detected in 14/28 anesthetic events. Atipamezole (5 mg per mg medetomidine) was injected intramuscularly for reversal 98±28 and 94±40 min after darting in juveniles and adults, respectively. Mean±SD time from administration of atipamezole to coordinated walking was 38±20 min in juveniles and 41±21 min in adults. Recovery was uneventful in 25 anesthetic events, although vomiting was observed in five animals. One adult that did not respond to atipamezole was given intravenous fluids and was fully recovered 8 hr after darting. Two animals died 7–9 hr after capture, despite intensive care. Both mortalities were attributed to shock and circulatory collapse following stress-induced hyperthermia. Although effective, this combination cannot be recommended for darting free-ranging wolves from helicopter at the doses presented here because of the severe hyperthermia seen in several wolves, two deaths, and prolonged recovery in one individual.

Key words: Anesthesia, atipamezole, *Canis lupus*, gray wolf, immobilization, ketamine, medetomidine.

Free-ranging gray wolves (*Canis lupus*) are anesthetized by darting from helicopter for various research and management purposes. Tiletamine-zolazepam has been used in free-ranging gray wolves for 20 yr and is currently the recommended immobilizing combination (Kreeger and Arnemo, 2012). Tiletamine-zolazepam has a wide safety margin in gray wolves. However, tiletamine is a potent anesthetic with a long elimination time and with no available antagonist. Consequently, prolonged recoveries, hypothermia, attacks from other wolves, poaching, suffocation in deep snow, drowning, and traffic accidents are major postcapture concerns.

Medetomidine-ketamine and atipamezole have been used for reversible immobilization and anesthesia in a range of carnivore species, including gray wolves in captivity (Holz et al., 1994). We report the use of these drugs in free-ranging gray wolves.

Free-ranging gray wolves were captured in south-central Scandinavia (11–15°E, 59–62°N). Wolf capture was approved by the Ethical Committee on Animal Experiments, Uppsala, Sweden, and by the National Animal Research Authority, Oslo, Norway. Target animals varied depending on study goals, but in most cases the target animals were preselected and tracked on the ground before helicopter tracking. Wolves were chemically immobilized in winter (10–40 cm snow depth; ambient temperature from −5 C to −15 C) from a helicopter using a CO_2-powered rifle and 3 mL lightweight plastic darts fitted with a 1.5×25 mm barbed needle with side ports (Dan-Inject®, Børkop, Denmark). From January 2002

TABLE 1. Summary statistics for 23 anesthesia events in free-ranging Scandinavian gray wolves (*Canis lupus*). Animals were darted from a helicopter during winter (December–March) in 2002 and 2003 with a standard dose of 5 mg medetomidine and 250 mg ketamine per animal. Each animal received atipamezole at 5 mg per mg of medetomidine intramuscular for reversal.

	Adults (>19 mo)				Juveniles (7–10 mo)			
Parameter	*n*	Mean	SD	Range	*n*	Mean	SD	Range
Body mass (kg)	17	44.0	5.0	35.0–52.0	6	31.0	1.5	29.5–33.5
Medetomidine (mg/kg)	17	0.114	0.013	0.096–0.143	6	0.162	0.008	0.149–0.169
Ketamine (mg/kg)	17	5.8	0.7	4.8–7.1	6	8.1	0.4	7.5–8.5
Induction time (min)	17	3.9	1.7	1.0–8.0	6	2.3	0.8	1.0–3.0
Duration (min)[a]	17	84	27	55–135	6	98	28	67–147
Head up (min)[b]	16	4.9	4.5	1–15	6	3.6	1.8	1–6
On feet (min)[b]	16	14	13	1–46	6	9	3	5–13
Walking (min)[b]	15	26	20	1–64	6	21	16	8–39
Leaving (min)[b]	15	45	20	25–81	6	38	20	18–60

[a] Time from darting to administration of atipamezole.

[b] Time from administration of atipamezole to lifting of the head, standing, walking, and leaving the area, respectively.

to December 2003, a standard dose of 5 mg of medetomidine (Zalopine® 10 mg/mL, Orion Pharma Animal Health, Turku, Finland) and 250 mg of ketamine (Narketan 10® 100 mg/mL, Chassot, Dublin, Ireland) per animal was used for 28 anesthetic events (9 adult [>19 mo old] females, 13 adult males, 6 juvenile [7–10 mo old] females) of 24 individual wolves. Four wolves were captured twice in separate winters. Induction time was the time (minutes) from darting to recumbency. Immobilized animals were transported by helicopter to a preselected handling site within several kilometers, placed on an insulated blanket, given a physical examination, and weighed, and depth of anesthesia was assessed via palpebral reflex, reaction to handling, jaw tone, and muscle relaxation. Rectal temperature (RT) was monitored with a digital thermometer, respiratory rate was determined by counting chest movements, and pulse and relative arterial oxygen saturation (SpO_2) were monitored by pulse oximetry (Nellcor® 20P, Nellcor Inc., Pleasanton, California, USA) with the sensor applied to the tongue. After processing, wolves were carried away from roads/human structures, and atipamezole (Antisedan® 5 mg/mL, Orion Pharma Animal Health) was administered intramuscularly at 5 mg per mg of medetomidine. Wolves were observed during recovery and the times from administration of atipamezole to lifting of the head, standing, walking, and leaving were recorded. Follow-up radiotelemetry (GPS or very high frequency collars) was carried out to assess postcapture survival. Necropsies were done at the National Veterinary Institute, Uppsala, Sweden. Statistical analysis was done, and the Mann-Whitney test was used to compare groups whereas the Wilcoxon test was used to compare repeated measurements within groups. We used $P<0.01$ to ascribe statistical significance.

Anesthetic events from five adults were excluded because they received more than one dart or additional drugs. One female was darted four times because the first three darts bounced off. One male was given 3 mg of medetomidine intramuscularly by hand-syringe injection 17 min after darting. One female was given 1 mg of medetomidine intravenously 19 min after darting because of signs of spontaneous recovery. Two males received additional doses of 1 mg of medetomidine intravenously 71 and 97 min, respectively, after darting to extend immobilization. Summary statistics for 23 immobilizations are given in Table 1. No differences were found between adult males (46±3.5 kg) and adult females (39±3 kg) regarding induction time, physiologic variables, or recovery parameters, and the results for adults were pooled. In general, inductions were rapid and calm, muscle relaxation was good, and there was no reaction to handling or minor painful stimuli. The palpebral reflex was present in all animals during immobilization.

The mean induction time was significantly shorter in juveniles than in adults. All animals except one adult female and one adult male were completely anesthetized after one dart. No significant differences in physiologic values between adults and juveniles were found, and there were no significant differences in other physiologic parameters between the first and last recording within the two age groups. There were no significant differences in induction time, physiologic variables, or recovery parameters between naïve (n=14) and recaptured (n=14) wolves. Mean±SD RTs recorded at 15–20, 25–30, 45–60, and 75–90 min after darting were 41.1±1.0, 40.7±1.0, 40.2 ±1.0, and 39.9±1.1 C in adults and 41.0±0.8, 40.8±0.6, 40.5±0.6, and 40.0±0.8 C in juveniles. Early and severe hyperthermia (≥41.0 C) was seen in three juveniles, two adult females, and nine adult males. The mean RT decreased significantly in both adults and juveniles during anesthesia.

Apart from vomiting in five wolves, recoveries were uneventful in 25 out of 28 immobilizations. One adult male (RT 41.9–39.9 C) that was still heavily sedated 4 hr after administration of atipamezole was given 1.5 L Ringer acetate solution and retreated with the full atipamezole dose subcutaneously and was fully recovered 2 hr later. One adult male (RT 42.0–41.7 C) never recovered and died 7 hr after darting, despite intensive care at a veterinary clinic. Necropsy showed poor body condition, a hemorrhagic inflammation throughout the gastrointestinal tract, and circulatory collapse. The female (RT 42.0–40.4 C) that was darted four times did not recover and was brought to a veterinary clinic for intensive care. No improvement occurred and the wolf was euthanized 8 hr after darting. Necropsy showed shock with circulatory collapse and multiple hemorrhages in intestines, liver, heart, spleen, lungs, and adrenal glands. The necropsy diagnosis for both wolves was shock and circulatory collapse with hemorrhagic gastroenteritis.

In addition to the two animals that died during anesthesia, four others died within 6 mo. One adult male was illegally killed after 2 days. Another adult male disappeared after 1 mo, presumably because of illegal hunting. A third adult male was shot after attacking livestock 3 mo later. A juvenile female drowned 2 mo postcapture. All other wolves survived at least 6 mo. Reproduction in the spring following capture was confirmed in three of four females in established pairs.

Immobilization and recovery were successful in 25 of 28 captures. Duration of immobilization was approximately 60 min or more in all six juveniles and in 17 of 19 adults that recovered normally. The mean dose for adults here was two times higher than those reported to be effective in captive gray wolves (Holz et al., 1994). Differences in effective doses are likely due to factors including psychologic condition, level of human habituation helicopter pursuit, and other stressors that are well documented in other wildlife species (Kreeger and Arnemo, 2012). Pursuit time could not be evaluated because wolves were running for variable amounts of time during snow tracking and before being spotted, and intensity of pursuit was also variable. The most common complication when anesthetizing free-ranging wolves is hyperthermia (Kreeger, 2003). The normal range for RT in free-ranging gray wolves is unknown, but in captive individuals the deep body temperature varied from 39.6 C during sleep to 40.2 C while running (Kreeger, 2003). Constable et al. (1998) reported a mean RT of 38.4 C in 11 free-ranging wolves immobilized with tiletamine-zolazepam from a helicopter.

Although the mean RT in our wolves (pooled data for all animals) was not extremely high, decreasing from 40.9 C initially to 39.8 C immediately before reversal, in 14 of 28 immobilizations, wolves were severely hyperthermic with initial RTs of 41.0–42.0 C, which is an emergency situation requiring aggressive treatment or immediate reversal (Kreeger and Arnemo, 2012).

Hypoxemia is common during wildlife immobilization, and oxygen should be administered to maintain an SpO_2 over 90% (Kreeger and Arnemo, 2012). Although a steady increase in SpO_2 from 82% to 88% was seen in both juveniles and adults during immobilization in the present study, most animals were hypoxemic, and evaluation of treatment with supplemental oxygen is warranted. Hypoxemia could have undetected undesirable effects, including organ dysfunction, for example in brain, liver, and kidneys (Gutierrez, 2006). These effects are difficult to evaluate in wildlife but may have consequences for the quality of results of ecologic studies dependent on capturing representative animals.

Our data showed steady but slightly decreasing mean pulse rates of 140–100 beats/min during immobilization, higher than the reported mean heart rate (65 beats/min) in captive wolves immobilized with medetomidine-ketamine (Holz et al., 1994) but similar to the heart rates in resting (84 beats/min) and interacting (159 beats/min) captive wolves (Kreeger, 2003). Mean respiratory rates in our wolves (16–21 breaths/min) were slightly higher than mean values reported in captive wolves immobilized with medetomidine-ketamine (12–17 breaths/min; Holz et al., 1994). Vomiting with subsequent asphyxiation has caused deaths in captured free-ranging wolves during both induction and recovery (Mark McNay, pers. comm.). Although no vomiting occurred during induction or immobilization in our study, five wolves vomited during recovery. Therefore, we recommend that wolves immobilized with medetomidine-ketamine be closely monitored until completely recovered.

In combination with xylazine (95–165 mg), doses of 600–850 mg of ketamine were used in 142 captures of free-ranging gray wolves in Alaska (Adams et al., 2008). Because of the potentiating effect of medetomidine, the dose of ketamine in our study (250 mg) was 60–70% lower than in the xylazine-ketamine combination. The 60–70% lower ketamine dose reduces drug volume and possible side effects of ketamine, and makes immobilization more reversible. Medetomidine-ketamine combinations have been used in a variety of other carnivores, including red fox (*Vulpes vulpes*) and golden jackals (*Canis aureus*) (Kreeger and Arnemo, 2012). In both red fox and golden jackals, animals were caught in leghold traps and lower doses could be used.

The duration of handling is affected by a variety of factors, including induction time, snow conditions and terrain for retrieving the animal, and the level of sampling conducted. Samples were collected for other studies, resulting in longer anesthesia times. In our study, the mean times from administration of atipamezole to when the animals were walking and then leaving the area (pooled data for 25 individuals) were 22.5 and 40.0 min, respectively. In free-ranging gray wolves immobilized with tiletamine-zolazepam, recovery may take 6–8 hr (Arnemo, pers. obs.).

In this study, two wolves died and one did not recover as expected. On necropsy, both mortalities were determined to be likely caused by shock and circulatory collapse following stress-induced hyperthermia. The death of one individual may have been secondary to hemorrhagic gastrointestinal inflammation and general poor condition, whereas multiple darts with possible drug overdosing may have aggravated the stress response in the other. The cause of extended recovery in one wolf is not known, but this wolf recovered completely and was living 6 mo postcapture. Because of severe hyperthermia in several wolves, death of two animals, and extended recovery in one individual, this combination is not recommended for aerial darting of free-ranging wolves at the doses presented here.

LITERATURE CITED

Adams LA, Stephenson RO, Dale BW, Ahgok RT, Demma DJ. 2008. Populations dynamics and harvest characteristics of wolves in the central Brooks Range, Alaska. *Wildlife Monogr* 170:1–25.

Constable P, Hinchcliff K, Demma N, Callahan M, Dale B, Fox K, Adams L, Wack R, Kramer L. 1998. Electrocardiographic consequences of a peripatetic lifestyle in gray wolves (*Canis lupus*). *Comp Biochem Physiol A* 120:557–563.

Gutierrez G. 2006. Hypoxia and hypoxemia. In: *Encyclopedia of respiratory medicine*, Geoffrey JL, Steven DS, editors. Oxford Academic Press, Oxford, England, pp. 302–307.

Holz P, Holz RM, Barnett JEF. 1994. Effects of atropine on medetomidine ketamine immobilization in the gray wolf (*Canis lupus*). *J Zoo Wildl Med* 25:209–213.

Kreeger TJ. 2003. The internal wolf: Physiology, pathology, and pharmacology. In: *Wolves. Behavior, ecology, and conservation*, Mech LD, Boitani L, editors. University of Chicago Press, Chicago, Illinois, pp. 192–217.

Kreeger TJ, Arnemo JM. 2012. *Handbook of wildlife chemical immobilization*, 4th Ed. Terry J. Kreeger, Sybille Canyon, Wyoming, 432 pp.

Submitted for publication 30 December 2011.
Accepted 19 September 2012.