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Butorphanol-Azaperone-Medetomidine for the Immobilization of Captive Caribou (*Rangifer tarandus granti*) in Alaska, USA

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ABSTRACT: A combination of butorphanol-azaperone-medetomidine was used to immobilize four captive caribou (*Rangifer tarandus granti*) in Palmer, Alaska, US. The average induction time for this combination was $5:17 \pm 2:06$ min. Inductions were smooth, and recoveries were excellent. This drug combination may provide an alternative to the use of potent opioids for immobilizing caribou.

Historically, combinations of carfentanil and xylazine (CX) or thiafentanil, azaperone, and xylazine (TAX) have been used to immobilize barren-ground caribou (*Rangifer tarandus granti*; Glenn 1967; Valkenburg et al. 1999; Lian et al. 2016). However, both carfentanil and thiafentanil are opioid analogs of fentanyl and are among the most potent opioids known (Kreeger and Arnemo 2012). Both of these drugs have been valuable tools for wildlife professionals but are very dangerous, and abuse among humans is increasing. The manufacture and sale of carfentanil was discontinued in June 2016. Thiafentanil is available only as a US Food and Drug Administration indexed product, Thianil (thiafentanil oxalate), and is restricted from extra-label uses. In addition to hazards for wildlife professionals that handle these drugs, both carfentanil and thiafentanil are major respiratory depressants (Kreeger and Arnemo 2012). For all these reasons, finding alternatives to these potent opioids is prudent.

Xylazine is an α -2 adrenergic agonist used in the CX and TAX combinations because it is a sedative, analgesic, and muscle relaxant. Side effects of α -2 adrenergic agonists include respiratory depression and hypoxemia, which are seen when using this drug in wild ungulates (Evans et al. 2013; Lian et al. 2014, 2016). Decreasing the dosage of α -2

adrenergic agonists used in wild ungulates would lessen these side effects.

A combination of butorphanol (27.3 mg/mL), azaperone (9.1 mg/mL), and medetomidine (10.9 mg/mL) is available commercially (BAM[™], Wildlife Pharmaceuticals, Inc., Windsor, Colorado, USA). Butorphanol is a partial opioid agonist-antagonist with a wide therapeutic margin and minimal cardiovascular effects (Kreeger and Arnemo 2012). Azaperone is a short-acting butyrophenone tranquilizer that may increase respiration and has minimal cardiovascular effects (Kreeger and Arnemo 2012). Medetomidine is a selective α -2 adrenergic agonist with sedative and analgesic properties. The important advantages that BAM offers over CX and TAX are lessened side effects (respiratory depression, bradycardia, etc.) associated with each of the individual drugs (Mich et al. 2008), and the use of a US Drug Enforcement Agency schedule IV (butorphanol) opioid rather than a schedule II opioid (carfentanil or thiafentanil). When using the provided recommended dosage guidelines (Wildlife Pharmaceuticals 2016) for BAM in ungulates, the quality of anesthesia has been considered excellent; however, hypoxemia has been noted. The hypoxemia resolves with nasal oxygen insufflation (Mich et al. 2007; Miller et al. 2009; Wolfe et al. 2014).

Multiple species have been immobilized with BAM, including white-tailed-deer (*Odocoileus virginianus*; Mich et al. 2007; Miller et al. 2009), Rocky Mountain elk (*Cervus elaphus nelsoni*; Wolfe et al. 2014), and black bears (*Ursus americanus*; Wolfe et al. 2008). Additionally, the manufacturer has published dosages for a wide variety of wildlife species, including reindeer (*Rangifer tarandus taran-*

TABLE 1. Measured parameters for four captive adult female caribou (*Rangifer tarandus granti*) intramuscularly hand-injected with butorphanol-azaperone-medetomidine (BAM) in Palmer, Alaska, USA, August 2017. Respiratory rate, heart rate, arterial oxygen saturation via pulse oximetry (SpO₂), and rectal temperature are presented as mean \pm SD where more than one reading was taken. Otherwise a single value is presented.

| Animal ID | Age (yr) | Body weight (kg) | Induction time ^a (mm:ss) | Approach time ^b (mm:ss) | Down time ^c (mm:ss) | Recovery time ^d (mm:ss) | Respiratory rate (breaths/min) | Heart rate (beats/min) | SpO ₂ ^e before O ₂ (%) | SpO ₂ ^e after O ₂ (%) | Rectal temperature (C) |
|-----------|----------|------------------|-------------------------------------|------------------------------------|--------------------------------|------------------------------------|--------------------------------|------------------------|---|--|------------------------|
| "Tag" | 7 | 93.2 | 03:26 | 04:20 | 35:00 | 02:15 | 18 \pm 2.8 | 70 | 81.5 \pm 3.5 | 92.5 \pm 4.9 | 39.9 \pm 0.4 |
| C-214 | 5 | Unknown | 08:15 | 10:30 | 30:00 | 01:45 | 16 | 70 | ND ^f | 91.3 \pm 2.1 | 41.3 \pm 0.4 |
| C-215 | 5 | 106.8 | 05:14 | 06:15 | 26:05 | 02:30 | 20 \pm 0 | 75 \pm 7 | 88.5 \pm 2.1 | 95.8 \pm 0.5 | 40.3 \pm 0.2 |
| C-218 | 5 | 84.1 | 04:14 | 06:10 | 28:00 | 01:15 | 14 \pm 2.8 | 80 \pm 0 | 87 | 91.0 \pm 1.0 | 40.9 \pm 0.3 |

^a Time from hand injection with BAM to sternal recumbency.

^b Time from hand injection with BAM to crew approach.

^c Time from sternal recumbency to injection of reversal.

^d Time from injection of reversal agents to standing.

^e Percentage hemoglobin saturation with oxygen.

^f ND = not done.

du). This dose, however, was based on the immobilization of only two captive reindeer bulls (W. Lance pers. comm.).

We believe that it is prudent to further assess BAM for use in caribou. This combination has the potential to provide excellent immobilization while avoiding the use of potent opioids. Here we describe the immobilization of four captive caribou using this drug combination and show that it is a potential alternative to combinations that contain potent and dangerous opioids.

Four adult (5–7 yr of age) female caribou (weight 84.1–106.8 kg) housed in Palmer, Alaska, US (61°36′07″N, 149°07′02″W) were used in the study in August 2017. Each caribou received 2.0 mL of BAM (a total of 54.7 mg butorphanol, 18.2 mg azaperone, and 21.8 mg of medetomidine) intramuscularly in either the right or left quadriceps muscle by hand injection. For each animal, time to ataxia, sternal recumbency, crew approach, time of reversal administration, and time to standing recovery were recorded (Table 1). After an arterial blood gas sample was collected, intranasal oxygen insufflation was started between 13 and 19 min of recumbency. During immobilization, temperature, pulse, respiratory rate, and arterial oxygen saturation via pulse oximetry were recorded periodically (Table 1). Following sample collection and physical examination, each animal was weighed. The butorphanol and medetomidine were antagonized with 50 mg of naltrexone and 100 mg of atipamezole, respectively, intravenously (IV) via the cephalic vein. Time to standing and time to full recovery were recorded for each animal. All procedures were conducted under Animal Care protocol no. 2016-48 reviewed and approved by the Alaska Department of Fish and Game Division of Wildlife Conservation Animal Care and Use Committee.

Means and standard deviations were calculated where multiple recordings were taken for heart rate, respiratory rate, arterial oxygen saturation via pulse oximetry, and rectal temperature. The average induction time was 5:17 \pm 2:06 min, and the average recovery

time was $2:19 \pm 0:25$ min (Table 1). Inductions were considered smooth for all animals with one animal showing mild superficial muscle tremors. The recovery was considered excellent in all four animals. Caribou C-214 was given 250 mg flunixin meglumine (Bimeda-MTC Animal Health Inc., Cambridge, Ontario, Canada) IV to reduce the risk of exertional myopathy after noting an elevated rectal temperature (41.6 C).

Based on the three body mass measurements available, the dosages given ranged from 0.51 mg/kg to 0.65 mg/kg butorphanol, 0.17 mg/kg to 0.22 mg/kg azaperone, and 0.20 mg/kg to 0.26 mg/kg medetomidine. These calculated doses are higher than those published for white-tailed deer (0.34–0.43 mg/kg butorphanol, 0.27–0.36 mg/kg azaperone, 0.11–0.14 mg/kg medetomidine; Mich et al. 2008; Miller et al. 2009) and for elk (0.17–0.34 mg/kg butorphanol, 0.11–0.22 mg/kg azaperone, 0.07–0.13 mg/kg medetomidine; Wolfe et al. 2014).

This drug combination worked well in four captive caribou. All inductions were smooth, induction times were acceptable, and recovery times were excellent. All caribou remained sternal with their heads upright and were minimally responsive to stimulation. All animals had an elevated rectal temperature (Blix et al. 2011). The use of this drug combination should be evaluated in free-ranging animals. In a free-ranging situation, in order to reduce that risk of resedation, the atipamezole is recommended to be intramuscularly rather than IV route used in this captive study.

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