DOI: 10.7589/2016-05-118

Journal of Wildlife Diseases, 53(3), 2017, pp. 636–641

Immobilization of Asiatic Black Bears (*Ursus thibetanus*) with Medetomidine-Zolazepam-Tiletamine in South Korea

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ABSTRACT: The Asiatic black bear (*Ursus thibetanus*; ABB) is a globally endangered species for which a restoration program has been ongoing in South Korea since 2001. However, there is little information on immobilization protocols for ABBs. We evaluated the use of medetomidine-zolazepam-tiletamine for their immobilization. During 2005–13, we anesthetized 60 ABBs (32 males, 28 females; 7 mo to 12 yr old) with medetomidine 0.03–0.045 mg/kg and zolazepam-tiletamine 1.54–2.3 mg/kg; reversal of anesthesia was done with atipamezole 0.15–0.225 mg/kg administered intravenously alone or intravenously and intramuscularly (50:50). Mean (and SD) for physiologic collected for 373 immobilizations of at least 60 min were: time to sedation, 7.8 (5.4) min; anesthesia induction time, 13.7 (8.1) min; complete recovery time, 14.8 (12.4) min; respiratory rate, 14 (7) breaths/min; heart rate, 51 (16) beats/min; rectal temperature, 37.3 (1.3) C; and hemoglobin oxygen saturation, 88% (6%). Few cardiopulmonary side effects occurred during immobilization and adequate depth of anesthesia was maintained for >60 min without need for supplementation. The dosage and drug combination used was effective for immobilization of ABBs with minimal adverse effects on vital signs and can be recommended in most clinical applications.

Key words: Alpha-2 agonist, anesthesia, Asiatic black bear, immobilization, medetomidine, tiletamine, *Ursus thibetanus*, zolazepam.

Many drug combinations have been used for chemical immobilization of bears. Zolazepam-tiletamine (ZT), xylazine-zolazepam-tiletamine (XZT), and medetomidine-zolazepam-tiletamine (MZT) have been used widely. However, XZT has a longer recovery time than MZT and MZT provides better analgesia than does ZT. Thus, MZT is considered superior to ZT and XZT in the field, especially in extreme temperatures (Caulkett and Fahlman 2014). The MZT combination has been used for brown bears (*Ursus arctos*; Evans et al. 2012), American black bears (*Ursus americanus*; Caulkett and Cattet 1997), and polar bears (*Ursus maritimus*; Cattet et al. 1997). Additional advantages of the MZT combination include the small volume required for remote delivery and reversibility using atipamezole following completion of clinical procedures. However, there is little information on anesthetic protocols in the Asiatic black bear (*Ursus thibetanus*; ABB) except for the application of ZT (Asano et al. 2007) or detomidine-ZT (Laricchiuta et al. 2008). We evaluated the utility of MZT and atipamezole for reversible immobilization of free-ranging and captive ABB.

As part of the endangered species restoration project run by the Ministry of Environment in South Korea, 60 ABBs (32 males, 28 females; 7 mo to 12 yr old) were anesthetized on 422 occasions during 2005–13 for health examination, attachment of radio transmitters, translocation of problem bears, and emergency rescue, both in the wild (Jirisan National Park, 35°12′40″–35°26′40″N and 127°27′20″–127°49′40″E) and in captivity (Species Restoration Technology Institute, Gurye, Republic of Korea).

We analyzed 373 anesthesia events each lasting 60–65 min. Each event was treated as an independent set of data, although some bears were captured on multiple occasions. Bears recaptured within 6 mo of a previous anesthetic event were excluded from the analysis. We used three capture methods for immobilization of free-ranging bears. The first method involved using a remote drug delivery system when the bears climbed a tree or did not continue to move after tracking by radio telemetry. The second method involved use of a baited culvert trap and the third involved

capturing the bear in its winter den during hibernation. The bears were anesthetized with intramuscular injections of zolazepam-tiletamine (1.5–2.3 mg/kg, Zoletil 50®, Virbac, France) and medetomidine (0.03–0.05 mg/kg, Domitor®, Pfizer, New York, New York, USA), at a distance of 5–20 m, using a CO_2-powered pistol with a 13-mm barrel and 5-mL or 10-mL darts containing 2×30-mm barbed needles with side ports (Dan-inject, Børkop, Denmark). Bears were weighed using a digital scale (Caston-1, CAS, Seoul, Korea) for calculation of drug dosages.

For each immobilized bear, the heart rate (HR), respiratory rate (RR), rectal temperature (RT), and percentage hemoglobin oxygen saturation (SpO_2) were recorded at 5-min intervals for 60 min. The HR, RT, and SpO_2 were measured using a patient monitor (Vet/Ox G2 Digital monitor, Heska, Fort Collins, Colorado, USA) and RR was measured by observing thoracic movements. After completion of the procedure, atipamezole (Antisedan®, Pfizer) was administered intravenously alone or both intravenously and intramuscularly (50:50) according to the bear's state of arousal at a dosage of 0.15–0.225 mg/kg, which was five times the administered dosage of medetomidine, and the animals were closely monitored for a minimum of 60 min to ensure that the circulating medetomidine was fully antagonized and to avoid resedation. We recorded time to sedation (time from initial injection to recumbency), anesthesia induction time (AIT; time from initial injection to complete immobilization without pedal or corneal reflex and full muscle relaxation), time to partial recovery (TPR; time from antagonist injection to raising of the head), and time to complete recovery (TCR; time from antagonist injection to dog-sitting posture or standing on four legs). The effects of season (hibernation, January–March; active state, April–December), habitat (wild or in captivity), sex, and age (cub=$<$2 yr; subadult=2–3 yr; adult=$\geq$4 yr) on vital signs (HR, RR, RT, and SpO_2) and times pertaining to anesthesia (time to sedation, IT, TPR, and TCR) were analyzed using Statistical Package for the Social Sciences 18.0 software (SPSS Inc., Chicago, Illinois, USA). All analytes were tested to confirm normal distribution using a Kolmogorov-Smirnov test. Season, habitat, and sex were analyzed using the independent *t*-test. Age was tested by one-way analysis of variance followed by Tukey's multiple comparisons test to detect significant variability between animals. All data are expressed as the mean and SD, and $P<0.05$ was considered statistically significant.

Anesthesia-related times, vital signs, body weight, and drug dosages are presented in Table 1. Time to sedation and AIT were significantly shorter in cubs and subadults than in adults, and TCR tended to be shorter in cubs than in adults; however, there was no significant age-related difference in TCR. The RR was lower in adults than in subadults and cubs. The HR in cubs was higher than in subadults and adults. The RT in adults was lower than in cubs. There was no significant age-related difference in SpO_2. Time to sedation and AIT were longer and TPR and TCR were shorter in female bears. There were no sex-related differences in HR, RR, and RT. However, SpO_2 was higher in males. All anesthesia-related times were significantly longer and HR, RT, and SpO_2 were lower during hibernation than when the bears were active. However, there was no difference in RR between hibernation and nonhibernation periods. The AIT was shorter and TPR longer in wild than in captive bears. There was no statistically significant difference in vital signs between wild and captive bears. The RR decreased and SpO_2 increased significantly in the 60 min after induction of anesthesia, but HR and RT did not change during this time (Fig. 1).

We identified age-related differences in vital signs, anesthesia induction time, and recovery. Young animals tend to have higher metabolic rates with increased cerebral oxygen demand than do older animals that have smaller numbers of neurons and decreased neurotransmitter levels. Furthermore, age may affect hepatic metabolic and renal excretory rates of drugs, resulting in altered vital signs, anesthesia-related induction, and recovery times (Clarke et al. 2014). Differ-

TABLE 1. Anesthesia-related times, vital signs, body weight, and drug dosage according to age, sex, season, and habitat in Asiatic black bears (*Ursus thibetanus*) immobilized with medetomidine-zolazepam-tiletamine in South Korea, 2005-13.

	Age mean (SD)			Sex mean (SD)		Season mean (SD)		Habitat mean (SD)		
Parameter[a]	Cub (n=69)[b]	Subadult (n=82)[b]	Adult (n=222)[b]	Male (n=184)[b]	Female (n=182)[b]	Hibernation (n=62)[b]	Active state (n=298)[b]	Wild (n=69)[b]	Captive (n=87)[b]	Total (n=373)[b]
TS (min)[c,d]	6 (5)	6.4 (5.3)	9 (5.3)[e,f]	7.2 (4.9)	8.5 (5.8)	9.7 (7.4)	7.4 (4.8)	7.1 (6.1)	8.1 (4.6)	7.8 (5.4)
AIT (min)[c,d,g]	10.2 (6.9)	11.1 (7.1)	15.9 (8.2)[e,f]	12.6 (7.1)	14.9 (9)	17 (10.9)	13 (7.2)	12.3 (9.6)	14.2 (7.5)	13.7 (8.1)
TPR (min)[c,d,g]	7.4 (7)	7.9 (7.1)	7.7 (7)	8.34 (7.5)	7 (6.7)	9.4 (7)	7.3 (6.4)	9 (8)	7.2 (6.6)	7.7 (7)
TCR (min)[c,d]	12.8 (9)	13.5 (10)	16 (13.9)	15.9 (12.5)	13.8 (12)	18.9 (16)	14 (10.2)	15.8 (13)	14.5 (12)	14.8 (12.4)
RR (breaths/min)	17 (9)	15 (8)	13 (6)[e,f]	14 (8)	14 (6)	14 (9)	14 (6)	15 (8)	14 (6)	14 (7)
HR (beats/min)[d]	67 (18)	51 (16)[e]	47 (11)[e]	52 (16)	50 (15)	38 (11)	54 (15)	52 (18)	51 (15)	51 (16)
RT (C)[d]	37.9 (1)	37.5 (1.3)	37 (1)[e]	37.2 (1.3)	37.4 (1.2)	36 (1.4)	37.6 (1)	37.3 (1.5)	37.3 (1.2)	37.3 (1.3)
SpO_2 (%)[c,d]	90 (5)	89 (4)	87 (6)	89 (5)	86 (6.24)	85.5 (5)	88 (6)	88 (3)	87 (6)	88 (6)
E_weight (kg)	26 (14)	66 (22)	136 (33)	102 (54)	99 (52)	92 (42)	102 (55)	68 (35)	111 (54)	100 (53)
A_weight (kg)	27 (14)	72 (25)	143 (34)	110 (59)	102 (52)	102 (44)	107 (58)	70 (36)	118 (56)	106 (56)
A_med (mg/kg)	0.04 (0.011)	0.038 (0.008)	0.038 (0.006)	0.038 (0.007)	0.039 (0.008)	0.037 (0.007)	0.039 (0.007)	0.04 (0.01)	0.038 (0.006)	0.038 (0.007)
A_zt (mg/kg)	1.99 (0.56)	1.89 (0.4)	1.91 (0.29)	1.89 (0.36)	1.96 (0.4)	1.83 (0.38)	1.94 (0.38)	2 (0.5)	1.9 (0.33)	1.92 (0.38)

[a] TS = time to sedation; AIT = anesthesia induction time; TPR = time to partial recovery; TCR = time to complete recovery; RR = respiratory rate; HR = heart rate; RT = rectal temperature; SpO_2 = hemoglobin oxygen saturation; E_weight = estimated measurement of weight; A_weight = actual weight; A_med = actual medetomidine dosage; A_zt = actual zolazepam-tiletamin dosage.

[b] Sample size represents the number of immobilizations. $P<0.05$ was considered statistically significant.

[c] Significant difference between sexes.

[d] Significant difference between seasons.

[e] Significant difference from cub value.

[f] Significant difference from subadult value.

[g] Significant difference between habitat groups.

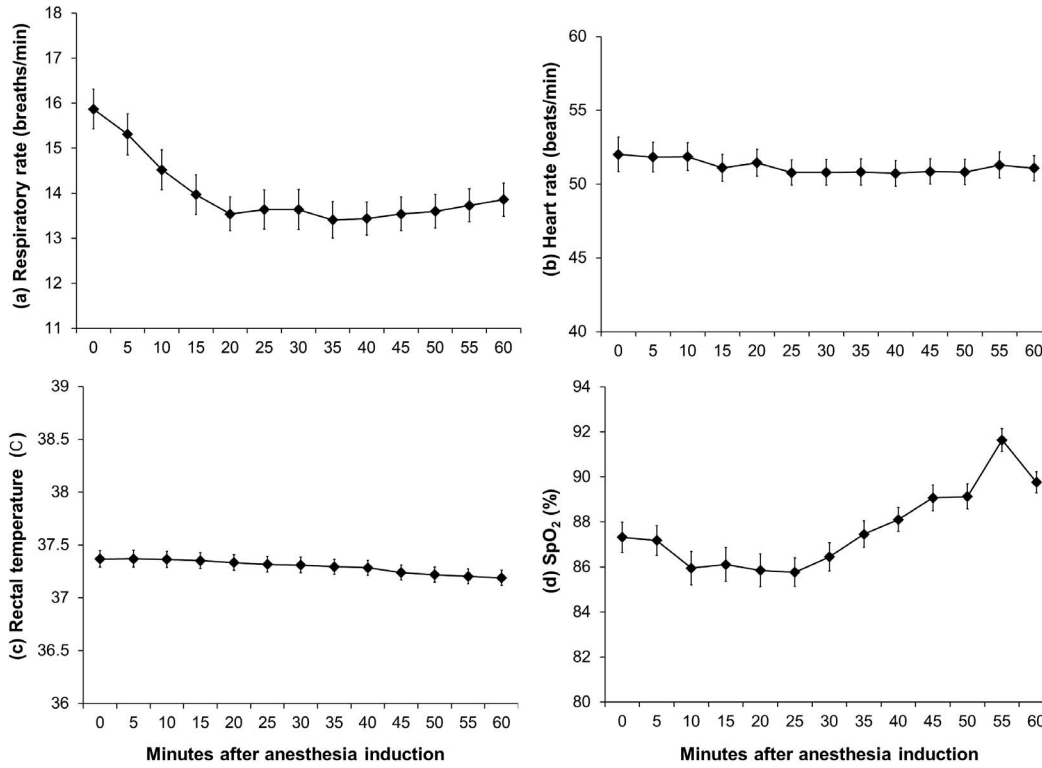

FIGURE 1. Total mean values for (a) respiratory rate, (b) heart rate, (c) rectal temperature, and (d) hemoglobin oxygen saturation (SpO_2) at 5-min intervals for Asiatic black bears (*Ursus thibetanus*) immobilized with medetomidine-zolazepam-tiletamine in South Korea, 2005–13. Respiratory rate decreased (t=4.37, df=137, P=0.001) and SpO_2 increased with time (t= –2.97, df=137, P=0.02). Bars = SE.

ences in physiologic variables between sexes associated with anesthesia have not been well investigated. We found that female bears had longer times to sedation and AIT values but shorter TPR and TCR values. The SpO_2 was the only physiologic variable that differed significantly between sexes. This may be related to a slightly higher mean corpuscular hemoglobin concentration in male than in female bears (Shanmugam et al. 2008), which indicates ability of greater oxygen delivery in males. However, more research in this regard is needed in the ABB to better understand anesthetic effects during hibernation and between sexes.

Anesthesia induction and recovery times were significantly longer and vital signs (except for RR) decreased during hibernation as compared to the active state. These changes are likely associated with reduced metabolic rate during hibernation (Tøien et al. 2011) and would lead to an increase in body fat just before hibernation. Our results are similar to those of others (Evans et al. 2012; Teisberg et al. 2014), except that we found no significant change in RR during hibernation. However, increased RR in our study may have been a compensatory response, with many immobilized bears during hibernation exhibiting irregular breathing depth and patterns, and the RR may have been an overestimation of the calculated thoracic movements. Evans et al. (2012) reported that it was possible to anesthetize hibernating brown bears using 25% of the doses used in summer. We used nearly equal doses to anesthetize bears in hibernation and nonhibernation periods. It is likely that the significantly higher RR during hibernation also would have been a result of

seasonal physiologic changes and relatively overdosed anesthetics.

The shorter anesthesia induction and longer recovery times in free-ranging bears compared to captive bears are probably related to differences in diet and physical activity. Captive bears receive regular high-calorie food but exercise was reduced due to limited space, so captive bears are expected to have higher body fat than would wild bears, which would alter drug metabolism, excretion, and distribution in the body, likely to influence the onset and offset of anesthesia. Medetomidine is a more potent alpha-2 agonist than is xylazine. Therefore, the adverse effects of drugs in this class, associated with adrenoceptor-drug dynamics, may be more pronounced, including cardiopulmonary activities. Adverse side effects may include decreased RR, hyperthermia (Radant 2009), and hypoxemia (Caulkett and Fahlman 2014). However, in our study, RT did not exceed 40 C and there were no clinically significant changes in RR. Further, total mean values of vital signs (HR, 50–90 beats/min; RR, 8–15 breaths/min; SpO_2, >85%; RT, 36.0–39.4 C) were within the ranges reported by other investigators (Radant 2009; Fahlman et al. 2011; Evans at al. 2012; Caulkett and Fahlman 2014). Additionally, we did not find any significantly different changes in vital signs over time that may be of clinical importance. Indeed, statistically significant RR decrease was only by 2 breaths in 60 min immobilization, and a meaningful analysis of the respiratory or ventilatory effect is difficult to derive without information on parameters such as oxygen, CO_2, and SpO_2 in the body. Increased SpO_2 over time may be due to improved ventilation resulting from increased drug metabolism and excretion with time, which had been observed in polar bears immobilized with MZT (Cattet et al. 1997).

Vomiting was documented in three captive bears in our study, despite the bears having been fasted for 24 h before anesthesia. However, these bears were from one family (a mother and two young cubs) and no episodes of vomiting occurred in the other bears. Thus, in this study, vomiting seemed to be a side effect of MZT experienced by a minority of ABBs. No other adverse side effects (excessive salivation, sudden arousal, resedation after recovery, death) were observed during immobilization. In conclusion, the immobilizations achieved using the anesthetic combination in our study provided a stable anesthetic plane with minimal adverse side effects except for transient mild hypoxemia. Supplementary oxygen via facemask or endotracheal intubation during immobilization would help prevent hypoxemia and improve the SpO_2 values. The anesthetic regimen, medetomidine 0.038 ± 0.007 mg/kg and zolazepam-tiletamine 1.92 ± 0.38 mg/kg, resulted in an effective immobilization of the Asiatic black bears and may be considered useful in most clinical applications.

We thank the staff of the Species Restoration Technology Institute, Korea National Park Service, for their assistance. We also thank Jonathan Sleeman, US Geological Survey National Wildlife Health Center, and Lyon Lee, Western University of Health Sciences for helpful comments and review on the manuscript.

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Submitted for publication 26 May 2016.
Accepted 12 January 2017.