Management and Conservation Note

Retention Time of Telazol in Black Bears

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ABSTRACT Telazol® (Fort Dodge Animal Health, Fort Dodge, IA) is an effective immobilization drug for American black bears (*Ursus americanus*), but concern exists regarding retention time of this drug in tissues relative to human consumption of bears. Therefore, we evaluated retention time of Telazol in captured American black bears immobilized with Telazol and held in captivity for 3 days, 7 days, 14 days, or 21 days. We detected Telazol in muscle and liver of one bear on day 7, in serum from 2 bears on day 7, and in urine of one bear each on day 3 and day 14. Our findings suggest Telazol is metabolized and eliminated quickly from the bear's system and should allow managers additional flexibility in mark–recapture studies and nuisance situations. (JOURNAL OF WILDLIFE MANAGEMENT 73(2):210–213; 2009)

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Telazol (1:1 mixture of tiletamine hydrochloride [HCl] and zolazepam HCl; Fort Dodge Animal Health, Fort Dodge, IA) is widely used to immobilize American black bears (*Ursus americanus*; hereafter, black bears) in nuisance and research situations. Telazol is effective and possibly the best immobilization drug currently available for black bears due to rapid induction and the bears' gradual and predictable recovery from immobilization (Bush et al. 1980, Gibeau and Paquet 1991, White et al. 1996). The Animal Medicinal Drug Use Clarification Act of 1994 requires veterinarians who prescribe extra label use of drugs to establish substantially extended withdrawal periods before possible human consumption of treated animals. Food animals immobilized with Telazol are an extra label use of this drug, and individual veterinarians must establish appropriate withdrawal times based on scientific information (Craigmill et al. 1997). Currently, many management agencies require euthanasia of black bears immobilized with Telazol within 45 days of hunting season due to uncertain retention times of Telazol and public health concerns associated with human consumption of meat from treated animals. The 45-day waiting period is not consistent among agencies and was only a suggested waiting time by most agencies because there is no published literature on retention time of Telazol in black bears. State agencies in West Virginia, North Carolina, Maryland, and some other states in the USA require a $\geq$45-day withdrawal period before possible human consumption of black bears immobilized with Telazol. The Canadian Cooperative Wildlife Health Centre suggests using 14 days for withdrawal times for all free ranging wildlife immobilized with Telazol as suggested by the Western Wildlife Health Committee of the Western Association of Fish and Wildlife Agencies (Canadian Cooperative Wildlife Health Centre 2002). However, they cite only one study on polar bears (*Ursus maritimus*; Semple et al. 2000) that reported low concentrations of tiletamine HCl and zolazepam HCl in polar bears between 0.5 days and 11 days after immobilization with Telazol, and they suggested that tissue levels of the drugs declined so rapidly that individuals consuming meat from exposed polar bears would be unlikely to experience negative effects from the drugs. The half-life of tiletamine and zolazepam in dogs was 1.2 hours and 1 hour, respectively (Baukema and Glazko 1975 as cited by Lin et al. 1993), whereas the half-life for tiletamine and zolazepam in polar bears was 1.8 hours and 1.2 hours, respectively (Semple et al. 2000). To address possible public health concerns and inform managers and administrators, we evaluated retention time in captured black bears immobilized with Telazol to determine a safe threshold for use of Telazol on black bears relative to potential human consumption.

METHODS

Personnel with West Virginia Division of Natural Resources and Virginia Department of Game and Inland Fisheries captured 15 (11 M, 4 F) wild black bears in nuisance situations in culvert traps and transported them to the Center for Bear Research at Virginia Polytechnic Institute and State University, Blacksburg, Virginia, USA, from 25 April 2005 through 19 August 2005. Mean weight and age were 104 kg ($n = 14$, range = 55–176 kg; Table 1) and 6.5 years ($n = 13$, range = 1–14 yr), respectively. Black bears we used in this research were destined to be destroyed for repeated or unacceptable nuisance activity. All methods were approved by the Institutional Animal Care and Use Committee (IACUC) at Virginia Tech (IACUC no. 05–053-F&W).

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Table 1. Concentrations (ppm) of tiletamine and zolazepam in serum, liver, muscle, and urine samples for black bears held for 3 days, 7 days, 14 days, and 21 days after immobilization with Telazol (Fort Dodge Animal Health, Fort Dodge, IA), in Virginia, USA (April–August 2005). We performed double tests on each sample when available.

				Serum		Liver		Muscle		Urine	
Day	Sex	Wt (kg)	Age (yr)	Tiletamine	Zolazepam	Tiletamine	Zolazepam	Tiletamine	Zolazepam	Tiletamine	Zolazepam
3	F	68	3	ND[a]	ND	ND	ND	ND	ND	0.090	ND
	F	68	3	ND	ND	ND	ND	ND	ND	0.080	ND
3	F	67	8	ND	ND	ND	ND	ND	ND	ND	ND
	F	67	8	ND	ND	ND	ND	ND	ND	ND	ND
3	M	166	6	ND	ND	ND	ND	ND	ND	ND	ND
	M	166	6	ND	ND	ND	ND	ND	ND	ND	ND
3	M	176	13	ND	ND	ND	ND	ND	ND	ND	ND
	M	176	13	ND	ND	ND	ND	ND	ND	ND	ND
7	M	83	2	ND	ND	ND	ND	ND	ND	ND	ND
	M	83	2	ND	ND	ND	ND	ND	ND	ND	ND
7	M	84	3	0.020	0.060	ND	0.032	0.015	0.014	NA[b]	NA
	M	84	3	0.020	0.060	ND	0.357	0.014	0.013	NA	NA
7	M	73	NA	ND	ND	ND	ND	ND	ND	ND	ND
	M	73	NA	ND	ND	ND	ND	ND	ND	ND	ND
7	M	114	5	0.160	0.600	ND	ND	ND	ND	NA	NA
	M	114	5	0.130	0.680	ND	ND	ND	ND	NA	NA
14	M	170	8	ND	ND	ND	ND	ND	ND	ND	ND
	M	170	8	ND	ND	ND	ND	ND	ND	ND	ND
14	M	139	12	ND	ND	ND	ND	ND	ND	ND	ND
	M	139	12	ND	ND	ND	ND	ND	ND	ND	ND
14	F	59	6	ND	ND	ND	ND	ND	ND	ND	0.060
	F	59	6	ND	ND	ND	ND	ND	ND	ND	0.060
14	F	66	14	ND	ND	ND	ND	ND	ND	ND	ND
	F	66	14	ND	ND	ND	ND	ND	ND	ND	ND
21	M	142	4	ND	ND	ND	ND	ND	ND	ND	ND
	M	142	4	ND	ND	ND	ND	ND	ND	ND	ND
21	M	55	1	ND	ND	ND	ND	ND	ND	NA	NA
	M	55	1	ND	ND	ND	ND	ND	ND	NA	NA

[a] Not detectable.
[b] Not available.

We immobilized black bears in culvert traps with 500 mg of Telazol, placed them in an individual holding facility (4.8 m in diam by 3.0 m tall) at the Center for Bear Research, and assigned each to 1 of 4 treatment groups: 3 days, 7 days, 14 days, or 21 days post-Telazol administration (Table 1). We immobilized each bear with 500 mg of Telazol because this most closely mimics field conditions of administering an entire bottle and should be the maximum amount needed to sedate an average-sized black bear. However, 2 black bears (T-5, a 165-kg M; and T-12, a 141-kg M) required 1,000 mg and 1,250 mg, respectively, to be immobilized so that we could safely handle them. Higher drug dosages are often used in wild animals to achieve more rapid inductions (Bush et al. 1980). We immobilized bears before removing them from culvert traps so exact weight was not known, but Telazol has a wide safety margin (Lin et al. 1993).

We fed each bear 1,000 g of high-protein dog food per day and provided water ad libitum. One male black bear (T-11) assigned to the 21-day group escaped from the facility 3 days before it was scheduled to be euthanized. For euthanasia, we first immobilized bears with a 2:1 mixture of ketamine/xylazine at 1 mL per 45.3 kg followed by euthanasia via pentobarbital by a veterinarian from the Virginia-Maryland Regional College of Veterinary Medicine (VMRCVM; Virginia Polytechnic Institute and State University, Blacksburg, VA) to collect samples. Pathologists at VMRCVM removed muscle (semimembranous muscle from the right rear leg), liver, serum, and urine samples (when available) and stored samples at −20° C.

In addition to black bears held at the Center for Bear Research, we also obtained blood samples from 6 live black bears as part of the West Virginia Division of Natural Resources' black bear research and monitoring program. These additional samples were useful to allow verification of extraction and analytical procedures and to determine accurate drug recoveries from serum that had high concentrations of Telazol. We collected samples exactly 1 hour after we immobilized each black bear with Telazol.

We processed all samples following procedures of Semple et al. (2000). Specifically, we added 1 g of serum or urine to 1 mL of a saturated aqueous solution of sodium bicarbonate and 50 µl of ketamine-d_4 (internal standard) in methanol to each falcon tube. We extracted the aqueous phase with ethyl acetate (3 × 2 mL) and back extracted the pooled organic phases with 2 mL of 0.1 M HCl. We basified the aqueous phase with a saturated aqueous solution of sodium bicarbonate (2 mL) and then extracted it with ethyl acetate (2 × 2 mL). We evaporated the solvent under nitrogen and reconstituted the residue in 100 µl of ethyl acetate and analyzed it by gas chromatography-mass spectrometry (GC-MS).

We added 1 g of muscle or liver tissue to 4 mL of a

saturated aqueous solution of sodium bicarbonate and 50 µl of ketamine-d_4 (internal standard, 10 ppm) in methanol to each glass tube. We homogenized and centrifuged the mixture and transferred the supernatant to a falcon tube. We extracted the aqueous phase with ethyl acetate (3 × 3 mL), back extracted pooled organic phases with 0.1 M HCl (2 × 2 mL), and basified the aqueous phase with a saturated aqueous solution of sodium bicarbonate (4 mL). We extracted the resultant solution with ethyl acetate (2 × 2 mL), evaporated the solvent under nitrogen, and reconstituted the residue in 100 µl of ethyl acetate and analyzed it by GC-MS.

We derived the standard calibration curve by adding serum, urine, or tissue to 100 µl of a mixture of tiletamine HCl and zolzepam HCl at concentrations of 0.1 ppm, 0.5 ppm, 1.0 ppm, 5.0 ppm, 10.0 ppm, and 50.0 ppm in water. We similarly processed serum, urine, and tissue the same way as these standard calibration samples. Each standard curve was linear throughout the range and had an R^2 value >0.99.

We analyzed all samples using a GC-MS system (Agilent Technologies, Wilmington, DE) equipped with a gas chromatograph model 6890 that was coupled to a model 5973 mass detector. We set operational parameters of the GC to an initial oven temperature of 120° C and held it there for 1 minute; we programmed oven temperature to increase at a rate of 25° C per minute until 300° C and then hold at 300° C for 408 seconds. We set front inlet temperature to 270° C, used helium gas as the carrier, and set the instrument for splitless mode with a constant flow rate of carrier gas of 1.5 mL/minute. The capillary column was an Agilent HP-5MS (5% phenyl methyl siloxane; 27.0 m × 0.25 m, at a film thickness 0.25 µm).

We set temperatures for the mass spectrometer detector (MSD) transfer line, quadripole, and source at 270° C, 150° C, and 230° C, respectively. We set the MSD acquisition parameters to an acquisition mode of single ion monitoring and a solvent delay of 4 minutes. We monitored the specific ions for the following compounds: tiletamine, 166.10 and 195.20, with a dwell time of 100 milliseconds; zolazepam, 257.20, 267.20, and 285.20, with a dwell time of 100 milliseconds; and ketamine-d4, 184.10 and 213.20, with a dwell time of 100 milliseconds.

RESULTS

Of the 14 captive black bears, we found detectable levels of tiletamine and zolazepam in the serum of 2 black bears in the 7-day group and trace amounts of either tiletamine or zolazepam in the urine of one 3-day and one 14-day black bear (Table 1). One black bear from the 7-day group was the only one of 14 sampled to have detectable levels of either tiletamine or zolazepam in its liver or muscle tissue. All 6 serum samples from live black bears had both tiletamine and zolazepam present in their blood (Table 2). Concentrations of both drugs were much higher in serum samples taken 1 hour after capture from live animals than those found in experimental bears.

Table 2. Concentrations (ppm) of tiletamine and zolazepam in serum from female black bears 1 hour after immobilization with Telazol (Fort Dodge Animal Health, Fort Dodge, IA), in West Virginia, USA, March 2005. We performed double tests on each sample when available.

Age (yr)	Tiletamine	Zolzepam
11	1.15	3.05
11	1.07	3.02
5	0.54	1.27
5	0.52	1.28
6	0.87	2.26
6	0.84	2.27
11	0.61	1.22
11	0.60	1.19
5	1.01	2.40
3	1.13	2.63
3	1.07	2.68

DISCUSSION

Our findings demonstrate that black bears are capable of quickly metabolizing and eliminating Telazol to undetectable levels within several (7–14) days and support the conclusions of Semple et al. (2000). High concentrations of Telazol in serum samples taken from live black bears 1 hour after immobilization revealed our ability to detect presence of tiletamine and zolazepam. We suggest that it is safe, from a public concern standpoint, to use Telazol to immobilize black bears up to 15 days before hunting seasons. However, certainty would require an experimentation study with increased sample sizes, which is unlikely from a practical standpoint. Of bears in the 14-day and 21-day groups, only one 14-day bear had trace amounts of zolazepam in its urine; all others had no detectable level of Telazol. Moreover, we only detected Telazol within muscle or liver tissue, the parts most likely to be consumed by humans, from one bear in the 7-day group. We held our black bears in captivity with limited mobility for a known number of days, which may have affected metabolism rates. However, our results concur with Semple et al. (2000) who used polar bears that were relocated and killed by hunters. Our results would not have concurred with Semple et al. (2000) if retention rates of tiletamine or zolazepam were strongly affected by activity level of bears, even though bears were different species.

Management Implications

Wildlife managers are often faced with an ever-increasing workload and limited time to complete their duties meaning that providing managers greater flexibility to conduct fieldwork is beneficial. Our results provide evidence that Telazol does not remain in a black bear's system for an extended period of time and that it is likely safe to immobilize black bears closer to hunting seasons than previously thought.

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