

## Optimal Medetomidine Dose When Combined with Ketamine and Tiletamine-zolazepam to Immobilize White-tailed Deer

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**ABSTRACT:** Chemical immobilization is often needed for safe and effective capture and handling of wildlife. We evaluated medetomidine (125, 150, 175, or 200 µg/kg; for synergistic effects and relaxation) mixed with ketamine (1.5 mg/kg; for relatively shorter recovery) and tiletamine-zolazepam (1.0 mg/kg; for rapid induction) in 22 female white-tailed deer (*Odocoileus virginianus*) at the University of Georgia Whitehall Deer Research Facility in Athens, Georgia, USA, on 14–15 and 21 May 2009. Deer were weighed before treatment, hand-injected intramuscularly (IM) while restrained in a squeeze chute, and released into a pen for monitoring. We measured rectal temperature, respiration rate, heart rate, hemoglobin saturation (using pulse oximetry), and arterial blood gases at 0, 10, and 20 min postimmobilization. We found no differences in induction time with different doses of medetomidine. Deer became laterally recumbent for all treatments combined at a median of 4.2 (2.6–21.3) min and were approachable by a median of 4.8 (3.5–21.8) min. Twelve of the 22 deer had rectal temperatures >40 C at time 0 and were treated with a cold-water enema. Hemoglobin saturation, estimated using pulse oximetry, was 79.5, 82.0, and 82.3% at times 0, 10, and 20, respectively. We injected atipamezole (0.35 mg/kg, IM) for reversal. Recovery occurred sooner and was more consistent for 125 and 150 µg/kg medetomidine whereby deer stood with minimal sedation to moderate ataxia within 60–90 min after atipamezole administration. We recommend using 150 µg of medetomidine with ketamine (1.5 mg/kg) and tiletamine-zolazepam (1.0 mg/kg) to provide effective and safe chemical immobilization of white-tailed deer.

**Key words:** Arterial blood gases, chemical immobilization, ketamine, medetomidine, *Odocoileus virginianus*, telazol, tiletamine-zolazepam, white-tailed deer.

Capture of free-ranging white-tailed deer (*Odocoileus virginianus*) by darting

requires safe and effective immobilizing drugs. The most successful drug regimens combine the synergistic effects of a tranquilizer, such as the  $\alpha_2$ -adrenergic agonist xylazine, with an anesthetic (Caulkett and Haigh, 2007), such as tiletamine-zolazepam. A commonly used combination includes xylazine with tiletamine-zolazepam (Caulkett and Haigh, 2007), but long reversal times may limit usefulness in the field (Miller et al., 2004). Ultrapotent opioids, including carfentanil, combined with xylazine have been evaluated; however, concern for human safety and undesirable side effects in deer (e.g., muscle rigidity and hyperthermia) have limited their use (Miller et al., 2003; Storms et al., 2005).

Medetomidine, an  $\alpha_2$ -adrenergic agonist, is 20–40 times more potent than xylazine and is readily reversed with atipamezole (Caulkett and Haigh, 2007). Medetomidine has been combined with butorphanol (analgesic) and azaperone (tranquilizer) to immobilize white-tailed deer (BAM; Miller et al., 2009). Medetomidine also has been combined with the anesthetic ketamine to immobilize white-tailed deer in captivity (Caulkett et al., 2000) and with clover traps (Millsbaugh et al., 2004).

Muller et al. (2007) found that ketamine-tiletamine-zolazepam (MKT) had potential for field immobilization of deer because of rapid induction and reduced reversal times. Use of the potent  $\alpha_2$ -adrenergic agonist medetomidine allowed the use of a lower dose of the anesthetics. We tested a range of medetomidine doses

to determine an optimal combination with ketamine and tiletamine-zolazepam (MKT) in captive deer, and we evaluated the quality and safety of each combination by monitoring physiologic parameters.

All animal procedures were approved by the University of Tennessee and University of Georgia Institutional Animal Care and Use Committees (UT-IACUC 1788 and UGA-IACUC A2007-10093-m1, respectively). Female deer (2–15 yr old) housed at the University of Georgia Warnell School of Forestry and Natural Resources Whitehall Deer Research Facility (33°53'N, 83°21'W) were moved from outside enclosures into individual 3×6-m barn stalls approximately 72 hr before immobilization, and they were weighed in a drop floor-type squeeze chute. We fasted all deer 12–16 hr before immobilization. We physically restrained each deer in the squeeze chute and hand-injected 1.5 mg/kg ketamine (100 mg/ml Ketaset®, Fort Dodge Animal Health, Fort Dodge, Iowa, USA), 1.0 mg/kg tiletamine-zolazepam (50 mg/ml tiletamine and 50 mg/ml zolazepam, 100 mg/ml total of Telazol®, Fort Dodge Animal Health), and either 125 (MKT-125), 150 (MKT-150), 175 (MKT-175), or 200 (MKT-200) µg/kg medetomidine (20 mg/ml, ZooPharm, Fort Collins, Colorado, USA) into its left hindquarter. After release into a 15×20-m observation pen, we measured time (seconds) to first effect (e.g., stumbling, changes in movements), to sternal recumbency (and did not rise again) and lateral positions (deer essentially immobile), and when we could approach the deer. We measured rectal temperature (B-D Digital Fever Thermometer, BD Biosciences, Franklin Lakes, New Jersey, USA), respiration rate (from thoracic movements), heart rate (auscultation), hemoglobin saturation (SpO<sub>2</sub>, using pulse oximetry; Rad-5 Masimo SET Handheld Pulse Oximeter, Irvine, California, USA), and arterial blood gases (IDEXX VetStat Analyzer, Westbrook, Maine, USA) at time of immobilization (time 0), and 10 and 20 min (time 10 and 20) after immobilization. We collected

<1 ml of blood from the auricular artery into heparinized syringes at times 0, 10, and 20 to measure arterial blood gases. At each sampling, we recorded arterial partial pressure of oxygen (PaO<sub>2</sub>, mmHg), arterial partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>, mmHg), total hemoglobin (g/dl), and blood pH.

After the last physiologic measurement, we moved each deer to an individual stall, administered the  $\alpha_2$ -antagonist atipamezole (0.35 mg/kg [5.0 mg/ml], Antisedan®, Pfizer Animal Health, Exton, Pennsylvania, USA) intramuscularly (IM), and monitored recovery. We recorded time to first effect (any indication of altered behavior), head-up, and standing, and then we recorded a sedation score every 30 min for 5 hr by using a scale of 0 (no sedation), 1 (minimal sedation with drooping eyelids), 2 (standing with moderate ataxia, braced stance, or lowered head carriage), 3 (sternal position but able to hold head up), 4 (lateral position without the ability to hold head up but still noticeable eye or ear movement), or 5 (lateral recumbency with no sign of reversal; Miller et al., 2004).

We tested timing and physiologic parameters for normality by using PROC UNIVARIATE using the Shapiro-Wilk test (SAS 9.2, SAS Institute, Cary, North Carolina, USA). We used nonparametric tests (PROC NPARIWAY, Kruskal-Wallis test; SAS Institute) to evaluate differences among medetomidine doses for induction and reversal time points because these values were found to violate the assumption of normality. We used a two-way analysis of variance and Duncan's multiple range test with time as a repeated measure for the physiologic parameters measured at times 0, 10, and 20.

There were no differences among medetomidine doses for time to first effect, sternal recumbency, lateral recumbency, or approach after injection of the immobilizing agents (Table 1). All deer, regardless of medetomidine dose, reached lateral recumbency by median of 4.2 (2.6–21.3) min and were approachable by a

median of 4.8 (3.5–21.8) min. There were no differences among medetomidine doses for first effect, head-up, or standing after reversal (Table 1).

Overall, mean heart rate remained stable (79, 81, and 72 beats per minute [bpm] at times 0, 10, and 20, respectively; Table 2) and within physiologic limits. Three, one, and six of 22 deer exhibited bradycardia (heart rate <60 bpm) at time 0, 10, and 20, respectively. Normal respiratory rate is 16–20 bpm. Respiratory rates were not normally distributed at 10 and 20 min but increased in all treatments and were significantly increased in MKT-200 (Table 2). Twelve of the 22 (55%) deer had a rectal temperature >40 C at time 0 (Table 2). All of these deer and one other deer (rectal temperature 39.1 C) were given cold-water enemas. Of these deer, five (23%) had rectal temperatures >41 C.

Hypoxemia (hemoglobin oxygen saturation <85%; Caulkett and Haigh, 2007) was a concern for most deer treated with all doses of medetomidine (Table 2). At times 0, 10, and 20, SpO<sub>2</sub> was 79.5 (SD=9.7), 82.0 (SD=8.5), and 82.3 (SD=7.8), respectively. Hypercapnia (PaCO<sub>2</sub>>60 mmHg; Storms et al., 2005) did not occur in any deer (Table 2). The pH tended to be greater for the middle range of medetomidine dose; however, deer were generally acidemic (pH<7.3; Storms et al., 2005). Bicarbonate (HCO<sub>3</sub><sup>-</sup>) increased over time (Table 2).

When combining all medetomidine doses, deer showed first signs of reversal after atipamezole injection at 4.3 (SD=4.4) min (Table 1). Deer raised their heads at 16.1 (SD=30.3) min. Deer treated with MKT-125 and -150 were able to stand with moderate ataxia to minimal sedation within 60–90 min (Fig. 1).

Induction compared favorably with other studies of white-tailed deer-immobilizing protocols evaluated at the same facility, including BAM-1 and BAM-2 (17.0 and 13.5 min, respectively; Miller et al., 2009), carfentanil-xylazine (4.7 min; Miller et al., 2003), and tiletamine-zolazepam-xylazine

TABLE 1. Timing of immobilization for captive white-tailed deer (*Odocoileus virginianus*) injected with ketamine (1.5 mg/kg), tiletamine-zolazepam (1.0 mg/kg), and different doses of medetomidine (125, 150, 175, or 200 µg/kg) and antagonized with atipamezole (0.35 mg/kg) at the University of Georgia Whitehall Deer Research Facility in Athens, Georgia, USA, on 14–15 and 21 May 2009.

Measurement <sup>a</sup>	125 µg/kg Medetomidine (n=6) <sup>b</sup>		150 µg/kg Medetomidine (n=5) <sup>b</sup>		175 µg/kg Medetomidine (n=6) <sup>b</sup>		200 µg/kg Medetomidine (n=5) <sup>b</sup>	
	Median	Range (n) <sup>b</sup>	Median	Range (n) <sup>b</sup>	Median	Range (n) <sup>b</sup>	Median	Range (n) <sup>b</sup>
Time to first effect (min)	1.6	1.2–2.3	1.6	1.2–3.6	2.1	1.7–2.6	2.2	2.1–2.4
Time to sternal recumbency (min)	2.8	2.2–5.0	2.8	2.6–14.0	3.3	2.7–5.3	3.3	2.8–3.9
Time to lateral recumbency (min)	4.3	3.0–5.5	3.9	2.6–21.3	4.0	3.3–5.8	4.4	3.8–4.8
Time to approach (min)	4.8	3.6–5.8	4.6	3.5–21.8	4.8	3.9–6.6	5.1	4.5–5.9
Time to first effect after reversal (min)	3.9	0.8–5.7	2.3	0.5–6.7 (3)	3.5	1.8–10.1	2.1	1.0–20.3
Time to head-up after reversal (min)	13.5	2.7–35.3	2.9	0.8–12.9 (3)	4.9	2.4–11.4	3.3	1.6–138.3
Time to standing after reversal (min)	27.6	3.5–37.0	12.7	2.0–31.5 (4)	22.4	3.5–31.0	36.7	4.1–57.5 (4)

<sup>a</sup> There were no significant differences by medetomidine dose for any measurement ( $P<0.05$ ).

<sup>b</sup> Sample size for each group unless otherwise noted in table.

TABLE 2. Physiologic parameters for captive white-tailed deer (*Odocoileus virginianus*) injected with ketamine (1.5 mg/kg), tiletamine-zolazepam (1.0 mg/kg), and different doses of medetomidine (125, 150, 175, or 200 µg/kg) at the University of Georgia Whitehall Deer Research Facility in Athens, Georgia, USA, on 14–15 and 21 May 2009.

Parameter <sup>a</sup>	Time <sup>b</sup>	125 µg/kg Medetomidine (n = 6) <sup>c,d</sup>			150 µg/kg Medetomidine (n = 5) <sup>c,d</sup>			175 µg/kg Medetomidine (n = 6) <sup>c,d</sup>			200 µg/kg Medetomidine (n = 5) <sup>c,d</sup>		
		Mean (SD)	Range (n) <sup>c</sup>	Mean (SD)	Range (n) <sup>c</sup>	Mean (SD)	Range (n) <sup>c</sup>	Mean (SD)	Range (n) <sup>c</sup>	Mean (SD)	Range (n) <sup>c</sup>		
Heart rate (bpm)	0 A	87.2 (14.1)	64.0–105.0	71.8 (18.5)	56.0–100.0	68.0 (8.8)	58.0–80.0	88.0 (14.2)	68.0–106.0				
	10 A	88.7 (18.4)	66.0–116.0	75.8 (18.5)	54.0–100.0	72.7 (5.5)	64.0–80.0	85.2 (10.1)	70.0–94.0				
	20 B	88.0 (24.3)	50.0–118.0	65.6 (20.6)	45.0–94.0	62.5 (6.5)	54.0–72.0	72.4 (7.3)	64.0–80.0				
Respiratory rate (bpm)	0	42.7 (18.6) B	24.0–78.0	33.4 (12.5) B	16.0–50.0	43.3 (16.7) B	22.0–66.0	77.6 (20.0) A	62.0–108.0				
	10	47.0 (23.3) B	30.0–92.0	32.8 (10.4) B	24.0–44.0	39.7 (25.3) B	20.0–86.0	65.8 (31.8) A	28.0–101.0				
	20	42.3 (25.5) B	20.0–88.0	27.4 (9.3) B	16.0–38.0	37.7 (25.3) B	18.0–86.0	62.8 (18.1) A	40.0–88.0				
Rectal temperature (C)	0	40.5 (1.2)	39.3–42.0	40.7 (1.5)	39.2–42.5	39.9 (0.8)	38.9–40.9	39.7 (0.6)	38.7–40.2				
	10	39.7 (1.2)	38.0–41.4	38.6 (2.1)	35.0–40.3	39.3 (1.1)	37.8–40.9	40.1 (0.9)	38.8–41.1				
	20	40.0 (1.2)	38.9–42.0	40.2 (0.3)	39.9–40.7	39.4 (1.3)	37.3–40.5	39.7 (1.0)	38.4–40.8				
SpO <sub>2</sub> (%) via pulse oximetry	0	80.2 (11.8)	58.0–89.0	77.4 (7.7)	66.0–84.0	80.7 (9.4)	69.0–93.0	79.6 (12.1)	63.0–94.0				
	10	86.3 (6.4)	80.0–95.0	81.0 (6.0)	73.0–89.0	77.2 (7.8)	69.0–92.0	83.8 (12.2)	65.0–93.0				
	20	81.5 (11.1)	62.0–93.0	82.0 (8.5)	75.0–95.0	82.7 (5.4)	78.0–90.0	83.0 (7.6)	71.0–89.0				
PaO <sub>2</sub> (mmHg)	0	55.2 (13.7)	43.0–77.0 (5)	49.2 (1.6)	47.0–51.0	55.5 (12.0)	40.0–69.0	64.3 (7.9)	56.0–75.0 (4)				
	10	61.6 (14.4)	47.0–78.0 (5)	46.8 (9.3)	35.0–60.0	48.0 (7.5)	41.0–56.0 (3)	57.8 (15.8)	42.0–78.0				
	20	62.2 (11.7)	53.0–76.0 (5)	48.8 (12.8)	34.0–60.0 (4)	51.6 (7.8)	43.0–62.0 (5)	57.0 (4.6)	52.0–61.0 (3)				
PaCO <sub>2</sub> (mmHg)	0 B	43.8 (7.3)	31.0–49.0 (5)	42.0 (3.4)	36.0–44.0	42.0 (7.4)	30.0–50.0	43.0 (4.1)	39.0–47.0 (4)				
	10 A	45.2 (6.4)	35.0–52.0 (5)	46.4 (3.4)	43.0–50.0	51.3 (3.1)	48.0–54.0 (3)	47.4 (4.3)	42.0–53.0				
	20 A	45.6 (7.1)	34.0–51.0 (5)	45.0 (2.6)	42.0–48.0 (4)	48.4 (5.3)	41.0–54.0 (5)	48.7 (5.7)	44.0–55.0 (3)				
HCO <sub>3</sub> <sup>-</sup> (Mmol/l)	0 C	16.1 (4.6)	9.1–24.4 (5)	20.1 (4.6)	15.5–25.5	17.7 (2.4)	14.3–20.4	16.5 (1.9)	14.7–18.4 (4)				
	10 B	17.4 (5.1)	11.1–24.4 (5)	23.2 (3.9)	17.8–27.3	20.1 (0.7)	19.4–20.7 (3)	19.9 (2.9)	16.9–24.3				
	20 A	19.4 (4.3)	14.0–24.0 (5)	24.8 (2.8)	22.0–28.5 (4)	21.5 (1.9)	18.3–23.2 (5)	21.0 (0.4)	20.6–21.3 (3)				
pH	0 B	7.20 (0.07) B	7.11–7.29 (5)	7.32 (0.09) A	7.19–7.42	7.27 (0.08) AB	7.20–7.42	7.22 (0.06) B	7.13–7.26 (4)				
	10 B	7.22 (0.07) B	7.15–7.31 (5)	7.33 (0.08) A	7.24–7.44	7.23 (0.04) AB	7.20–7.27 (3)	7.26 (0.05) B	7.20–7.33				
	20 A	7.27 (0.06) B	7.19–7.33 (5)	7.38 (0.05) A	7.33–7.44 (4)	7.29 (0.04) AB	7.25–7.34 (5)	7.28 (0.04) B	7.23–7.31 (3)				

<sup>a</sup> bpm = beats per minute; SpO<sub>2</sub> = hemoglobin saturation; PaO<sub>2</sub> = partial pressure of oxygen; PaCO<sub>2</sub> = partial pressure of CO<sub>2</sub>.  
<sup>b</sup> Means with the same letter within a column (for each parameter) were not significantly different (P>0.05). There was no interaction between time and medetomidine dose.  
<sup>c</sup> Sample size for each group unless otherwise noted in table.  
<sup>d</sup> Means with the same letter within a row (for each treatment) were not significantly different (P>0.05). There was no interaction between time and medetomidine dose.

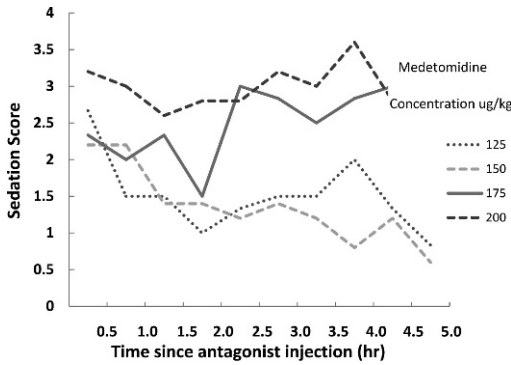


FIGURE 1. Mean sedation score for captive white-tailed deer (*Odocoileus virginianus*) injected with ketamine (1.5 mg/kg), tiletamine-zolazepam (1.0 mg/kg), and different doses of medetomidine (125, 150, 175, or 200 µg/kg) and antagonized with atipamezole (0.35 mg/kg) at the University of Georgia Whitehall Deer Research Facility in Athens, Georgia, USA, on 14–15 and 21 May 2009. Atipamezole was 2.8, 2.3, 2, and 1.8 times the medetomidine dose for MKT-125, -150, -175, and -200, respectively. Sedation score was recorded every half hour for 5 hr: 0 (no sedation), 1 (minimal sedation with drooping eyelids), 2 (standing with moderate ataxia, braced stance, or lowered head carriage), 3 (sternal position but able to hold head up), or 4 (lateral position without the ability to hold head up but still noticeable eye or ear movement).

(2.4 min; Miller et al., 2003). Evaluation of immobilizing chemicals with similar methods at the same research facility aided our understanding of the advantages and disadvantages for each combination. Butorphanol-azaperone-medetomidine minimized hyperthermia and was effective, but deer became mildly hypoxic and induction times were longer (Miller et al., 2009). Carfentanil-xylazine was effective but exhibited poor-quality inductions, with hyperthermia, acidemia, and muscle rigidity (Miller et al., 2003; Storms et al., 2005). Tiletamine-zolazepam-xylazine caused rapid induction with good physiologic parameters, but reversals were prolonged, regardless of antagonist used (Miller et al., 2004).

The combination of the potent  $\alpha_2$ -adrenergic agonist medetomidine combined with lower doses of two dissociative anesthetics provided rapid, smooth induction and acceptable reversal times, al-

though body temperatures were increased and most deer were hypoxic (Table 2). We treated each of these deer with a cold-water enema and did not see any adverse effects from the hyperthermia. In our study, ambient temperature ranged from 16.1 C to 29.4 C (National Climatic Data Center, 2009). Field use and future studies should avoid immobilizing animals on warmer days. Hypoxemia is a common problem in anesthetized deer (Caulkett and Haigh, 2007) and is particularly associated with the use of  $\alpha_2$ -adrenoreceptor agonists.

Carbon dioxide was not increased dramatically in the deer of this study, and decreases in pH were mainly due to metabolic acidosis, as demonstrated by a decrease in bicarbonate (Doherty and Valverde, 2006). Metabolic acidosis has been associated with capture and handling of animals because increased muscle activity promotes anaerobic oxidation and increased production of lactic acid often leading to capture myopathy. However, we did not see any signs of capture myopathy.

Overall, deer were slow to recover when given the antagonist. However, atipamezole should be 3–5 times the medetomidine dose (Caulkett and Haig, 2007). We used 0.35 mg/kg medetomidine dose for all concentrations of medetomidine; therefore, atipamezole was 2.8, 2.3, 2, and 1.8 times the medetomidine dose for MKT-125, -150, -175, and -200, respectively. Higher doses of atipamezole based on the medetomidine dose may have improved recovery times.

We recommend using the 150-µg/kg dose of medetomidine with ketamine (1.5 mg/kg) and tiletamine-zolazepam (1.0 mg/kg), a combination that was effective and allowed for faster and more consistent recovery (Fig. 1). We also suggest increasing the atipamezole dose to improve recovery and only immobilizing deer in cooler temperatures.

We received funding and support from Warnell School of Forestry and Natural Resources, University of Georgia, and the University of Tennessee, Knoxville. We

thank K. Amass for suggestions on methodology. We appreciate the field help of J. Beaver, M. Lashley, D. Baxter, W. Gulsby, S. Ellis Felege, G. Cash, B. Bennett, M. Cherry, D. Stull, A. Davis, V. Lane, G. Marsh, and A. Hecht.

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Submitted for publication 10 June 2011.

Accepted 1 November 2011.