Use of Xylazine/Ketamine or Medetomidine Combined with Either Ketamine, Ketamine/Butorphanol, or Ketamine/Telazol for Immobilization of White-Tailed Deer (Odocoileus Virginianus)

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Abstract: We immobilized 18 captive, adult, female white-tailed deer (Odocoileus virginianus) with a combination of either 1) xylazine/ketamine (XK; 1.6+0.1 mg kg⁻¹ xylazine and 7.8+0.3 mg kg⁻¹ ketamine antagonized with 2.1+0.1 mg kg⁻¹ tolazoline), 2) Medetomidine/Ketamine (MK; 0.075+0.01 mg kg⁻¹ medetomidine and 2.1+0.2 mg kg⁻¹ ketamine antagonized with 0.37+0.0 mg kg⁻¹ atipamezole), 3) Medetomidine/Ketamine/Butorphanol (MKB; 0.072+0.01 mg kg⁻¹ medetomidine, 2.1+0.2 mg kg⁻¹ ketamine and 0.1+ 0.0 mg kg⁻¹ butorphanol antagonized with 0.36+0.0 mg kg⁻¹ atipamezole and 10.3+1.2 mg kg⁻¹ naltrexone), 4) Medetomidine/Ketamine/Tiletamine-zolazepam-A (MKT-A; 0.063+0.0 mg kg⁻¹ medetomidine, 0.9+0.1 mg kg⁻¹ ketamine and 2.0+0.1 mg kg⁻¹ tiletamine-zolazepam antagonized with 0.31+0.0 mg kg⁻¹ atipamezole), or 5) Medetomidine/Ketamine/Tiletamine-zolazepam-B (MKT-B; 0.067+0.0 mg kg⁻¹ medetomidine, 1.4+0.1 mg kg⁻¹ ketamine and 1.1+0.1 mg kg⁻¹ tiletamine-zolazepam antagonized with 0.34+0.0 mg kg⁻¹ atipamezole). We measured times from injection to first effect, sternal recumbency and lateral recumbency. We measured SpO₂, heart rate, respiratory rate and body temperature of each deer at 20 and 40 min after lateral recumbency. Forty-five minutes after lateral recumbency, deer were given appropriate antagonist drugs (half i.v., half i.m.). All drug combinations except the XK dose produced lateral recumbency in the deer. Hyperthermia occurred in the XK, MKB and MK groups. The MKT-A and MKT-B treatments resulted in acceptable physiological parameters, rapid induction and quick recovery. Combining ketamine (for a relatively shorter recovery time), tiletamine-zolazepam (for rapid induction) and medetomidine (for synergistic effects and increased relaxation) may optimize induction and recovery times in white-tailed deer.

Key words: Butorphanol, ketamine, medetomidine, Odocoileus virginianus, tiletamine-zolazepam, white-tailed deer

INTRODUCTION

Capture of white-tailed deer (Odocoileus virginianus) is greatly facilitated by the use of potent immobilizing drugs. The characteristics of the ideal capture drug have been described as safe, short induction time, wide therapeutic index, no long-term effects, small volume for darting and reversibility (Nielsen, 1999; Kreeger et al., 2002; Miller et al., 2003). However, previously evaluated drug combinations require compromises among rapid induction and recovery times or other undesirable characteristics.

Xylazine plus Ketamine (XK) is commonly used for immobilization of white-tailed deer (Kreeger et al., 2002). However, shorter flight distances were found after darting deer with a combination of xylazine and tiletamine-zolazepam (XT) compared to XK (Kilpatrick and Sphor, 1999). Tiletamine/zolazepam combines a dissociative
anesthetic with a benzodiazepine tranquilizer. The main disadvantage of XT is the relatively long recovery times because the longer duration of action of tiletamine/zolazepam compared to ketamine (Miller et al., 2004). There is no antagonist available for the dissociative drugs and the use of different alpha antagonists (yohimbine, atipamezole, or tolazoline) did not affect the duration of sedation in white-tailed deer immobilized with XT (Miller et al., 2004). Additionally, flumazenil was not an effective antagonist for the zolazepam (Miller et al., 2004).

Alpha1-adrenoceptor agonists (e.g., xylazine and medetomidine) provide sedation, analgesia and muscle relaxation (Plumb, 2002). Medetomidine has 10 times the affinity for alpha1 versus alpha, receptors and greater potency than xylazine (Kreeger et al., 2002; Plumb, 2002). The greater receptor specificity and potency of medetomidine can lead to a reduction in the dose of dissociative agents required for immobilization and may make this drug a better choice for use with dissociative anesthetics in many species. Additionally, the antagonist, atipamezole, quickly reverses alpha 2-agonists and has a high specificity for medetomidine (Plumb et al., 2002).

Medetomidine alone provides effective sedation and immobilization for a variety of wildlife species including reindeer (Rangifer tarandus) and red deer (Cervus elaphus) (Jalanka and Roeken, 1990). However, variation in quality and depth of sedation are often seen and may be attributed to individual animal, species-specific or dose-dependent differences (Kumar et al., 1994). Ketamine or tiletamine-zolazepam are often combined with medetomidine to ensure more consistent immobilization and human safety (Jalanka and Roeken, 1990; Fernandez et al., 2000). The benzodiazepine, zolazepam, causes muscle relaxation and likely contributes to the relatively rapid induction and longer duration of XT effect (Kumar et al., 2006), compared to XK. Tiletamine is quickly cleared from the body and has lower peak concentrations in the blood compared to zolazepam (Kumar et al., 2006). Adding opioid analgesics such as butorphanol, to medetomidine plus ketamine or tiletamine/zolazepam may further shorten induction times. Greater muscle relaxation and deeper sedation was found in ring-tailed lemurs (Lemur catta) when combining butorphanol with medetomidine (Williams et al., 2003). Medetomidine/ketamine/butorphanol has been used successfully in Thomson’s gazelles (Gazella thomsoni) (Chittick et al., 2001).

In this study, we evaluated the effectiveness of XK and medetomidine combined with ketamine, ketamine/butorphanol, or ketamine/tiletamine-zolazepam for immobilizing captive white-tailed deer.

**MATERIALS AND METHODS**

All immobilizations were conducted with captive deer at the University of Georgia Daniel B. Warnell School of Forest Resources Whitehall Deer Research Facility (33°53’N, 83°21’W). Research protocols were reviewed and approved by the University of Tennessee and University of Georgia Animal Care and Use Committees (UT-ACUC 1431; UGA-ACUC A2005-10202-0).

We conducted trials during 11-13 April 2005 of 18 adult female deer (ages 3-12+ yr) randomly assigned to treatment group. The does were housed in outdoor pens with fertile bucks during the previous fall and winter (Miller et al., 2004). At 16-24 h before drug treatments, we moved them to individual 3×6-m barn stalls. We randomly selected four females and weighed them to the nearest kg in the squeeze chute to determine a standardized dosage rate to use for all deer (mean body weight = 54 kg). Deer were not fed for 12-16 h before treatments to minimize risk of regurgitation during immobilization. To minimize the risk of thermal stress during immobilization, we administered treatments during 0700-1200 h. No adverse effects were reported on pregnancy or neonatal survival in white-tailed deer immobilized with XK during pregnancy (from December to May, with mean parturition date of 8 June) (Delgadillo et al., 1986). Therefore, we expected no drug-related complications when our females were treated at 4-5 mo of gestation. However, to monitor potential treatment effects on fawning, we observed each female daily during May-July 2005.

Our drug trials included xylazine (100 mg mL⁻¹), Wildlife Pharmaceuticals, Inc., Fort Collins, Colorado 80522, USA), medetomidine (20 mg mL⁻¹, medetomidine hydrochloride, Wildlife Pharmaceuticals), ketamine (100 mg mL⁻¹, Ketaset®, Fort Dodge Animal Health, Fort Dodge, Iowa 50501, USA), butorphanol (10 mg mL⁻¹, Torbugesic®, Fort Dodge Animal Health), tiletamine/zolazepam (50 mg mL⁻¹ tiletamine and 50 mg mL⁻¹ zolazepam; 100 mg mL⁻¹ total of Telazol®, Fort Dodge Animal Health), atipamezole (5.0 mg mL⁻¹, Antisedan®, Pfizer Animal Health, Exton, Pennsylvania 19341, USA), naltrexone (50 mg mL⁻¹, Wildlife Pharmaceuticals) and tolazoline (100 mg mL⁻¹ Tolazip®, Lloyd Laboratories, Shenandoah, Iowa 51601, USA).

Drug dosage for a 54 kg deer was based on recommendations by Kreeger et al. (2002) for non-excited deer (due to relative adaptation to the facility and handling) unless otherwise noted. All Treatments included Xylazine/Ketamine (XK, 1.5 mg kg⁻¹ xylazine and 7.5 mg kg⁻¹ ketamine antagonized with 2.0 mg kg⁻¹ tolazoline), Medetomidine/Ketamine (MK, 0.07 mg kg⁻¹ medetomidine and 2.0 mg kg⁻¹ ketamine antagonized with
0.35 mg kg⁻¹ atipamezole), Medetomidine/Ketamine/Butorphanol (MKB: 0.07 mg kg⁻¹ medetomidine, 2.0 mg kg⁻¹ ketamine and 0.1 mg kg⁻¹ butorphanol, antagonized with 0.35 mg kg⁻¹ atipamezole and 10 mg kg⁻¹ naloxone dose), Medetomidine/Ketamine/Tiletamine-zolazepam-A (MKT-A: 0.07 mg kg⁻¹ medetomidine, 1.0 mg kg⁻¹ ketamine and 2.2 mg kg⁻¹ tiletamine-zolazepam antagonized with 0.35 mg kg⁻¹ atipamezole), Medetomidine/Ketamine/Tiletamine-zolazepam-B (MKT-B: 0.07 mg kg⁻¹ medetomidine, 1.5 mg kg⁻¹ ketamine and 1.1 mg kg⁻¹ tiletamine-zolazepam antagonized with 0.35 mg kg⁻¹ atipamezole).

We restrained each deer in a squeeze chute and administered drug treatments by i.m. injection in the left hindquarter. After injection, deer were released into a 15x20-m observation pen. One observer recorded time to first noticeable drug effect, sternal recumbency and lateral recumbency. Once recumbent, each deer was weighed (for determination of exact dose administered) and carried to an individual stall, treated with ophthalmic ocular lubrication (Paralube®; Pharmaderm, Mellerly, New York 11747, USA) to prevent corneal drying, eyes covered with a masked and held in a sternal position. At 20 and 40 min. after lateral recumbency, we recorded SpO₂ (pulse oximeter, Ohmeda Bix 3700, Ohmeda, Louisville, Colorado 80027, USA; probe placed on tongue), heart rate (determined by auscultation or from pulse oximeter), respiration rate (observed by thoracic movements) and rectal temperature. About 45 min. after lateral recumbency, deer were given the antagonists (half i.v. and half i.m.). We recorded time from antagonist administration to head up and standing for each deer. Starting at 30 min after antagonist injection, we recorded a sedation score which ranged from 0-5 (Miller et al., 2004) for each deer every 30 min for 5 h. The score was assessed as follows: lateral recumbency with no sign of reversal (5), lateral recumbency, unable to maintain the head upright and sensory movement of eyes or ears (4), unable to stand, disoriented and unsteady, but able to hold head erect (3), standing with moderate ataxia, spread stance, with head lowered occasionally (2), standing with minimal sedation characterized by lowered eyelids (1), no sign of sedation (0).

Statistical analysis was performed with SAS (SAS Institute, Cary, North Carolina 27513, USA). Treatment effects for each parameter were determined with one-way analysis of variance and Duncan’s Multiple Range Test for mean separation. Statistical significance was considered at p<0.05.

**RESULTS**

There were no differences in time to first effect (p = 0.06) or lateral recumbency (p = 0.61) among drug treatments (Table 1). However, time to sternal recumbency varied (p = 0.01) by drug treatment (Table 1). Subjectively, the XK deer were lightly sedated and one individual could not be approached, or moved. Three of the four MK deer responded to touch and would have been reactive to invasive procedures during immobilization. All remaining deer were effectively immobilized and unresponsive to touch.

Table 1: Mean signs of immobilization and recovery for 18 captive white-tailed does after administration of immobilizing drugs and appropriate antagonist, 11-13 April 2005, Athens, Georgia

<table>
<thead>
<tr>
<th>Drug Comb.</th>
<th>Immobilizing drug</th>
<th>Doseage mg kg⁻¹±SD</th>
<th>Antagonist dosage mg kg⁻¹±SD</th>
<th>Time to first effect* Seconds±SD (n)</th>
<th>Time to sternal recumbency* Seconds±SD (n)</th>
<th>Time to lateral recumbency* Seconds±SD (n)</th>
<th>Time to head up** Seconds±SD (n)</th>
<th>Time to standing** Seconds±SD (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>XK</td>
<td>1.6±0.1 xylazine</td>
<td>7.8±0.5 ketamine</td>
<td>2.1±0.1 tolazoline</td>
<td>315.6±48.0 (3) A</td>
<td>418.4±51.0 (3) A</td>
<td>569.4±32.7 (3) A</td>
<td>82.8±8.1 (2) A</td>
<td>75.9 (1) A</td>
</tr>
<tr>
<td>MK</td>
<td>0.07±0.01 medetomidine</td>
<td>0.37±0.0 atipamezole</td>
<td>184.8±32.5</td>
<td>418.4±51.0 (3) A</td>
<td>569.4±32.7 (3) A</td>
<td>82.8±8.1 (2) A</td>
<td>75.9 (1) A</td>
<td></td>
</tr>
<tr>
<td>MKB</td>
<td>0.072±0.01 medetomidine</td>
<td>0.36±0.0 atipamezole</td>
<td>116.3±14.6</td>
<td>250.0±14.8 (4) A</td>
<td>546.0±50.9 (3) A</td>
<td>140.0±9.7 (3) A</td>
<td>180.0±20.0 (3) A</td>
<td></td>
</tr>
<tr>
<td>MKT-A</td>
<td>0.063±0.0 medetomidine</td>
<td>0.31±0.0 atipamezole</td>
<td>174.5±42.9</td>
<td>284.8±57.3 (4) A</td>
<td>380.0±57.1 (4) A</td>
<td>315.0±29.4 (4) A</td>
<td>620.0±183.3 (3) A</td>
<td></td>
</tr>
<tr>
<td>MKT-B</td>
<td>0.067±0.0 medetomidine</td>
<td>0.34±0.0 atipamezole</td>
<td>175.0±34.7</td>
<td>275.3±68.0 (4) A</td>
<td>323.3±69.3 (4) A</td>
<td>510.0±82.0 (4) A</td>
<td>740.0±922.4 (3) A</td>
<td></td>
</tr>
</tbody>
</table>

*Means in the same column with different superscripts are significantly different (Time to first effect (p = 0.06), time to sternal (p = 0.01), time to lateral (p = 0.01), time to head up (p = 0.62), time to standing (p = 0.36))
Table 2: Mean values (± SD) of physiological parameters for 18 captive white-tailed does after treatment with immobilizing drugs, 11-13 April 2005, Athens, Georgia. Parameters were measured from the time deer were laterally recumbent.

<table>
<thead>
<tr>
<th>Drug</th>
<th>S&lt;sub&gt;O2&lt;/sub&gt;</th>
<th>Respiration rate breaths/min</th>
<th>Heart rate Beats/min</th>
<th>Temperature °C</th>
<th>Temperature ± SD (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X ±SD (n)</td>
<td>20 min</td>
<td>40 min</td>
<td>20 min</td>
<td>40 min</td>
</tr>
<tr>
<td>XCl</td>
<td>88.0±8.5 (2)</td>
<td>No data</td>
<td>No data</td>
<td>84.0±97.7 (2)</td>
<td>No data</td>
</tr>
<tr>
<td>MK</td>
<td>88.3±8.1 (3)</td>
<td>92.3±29.5 (3)</td>
<td>27.4±14.3 (4)</td>
<td>24.7±11.5 (3)</td>
<td>64.0±13.9 (4)</td>
</tr>
<tr>
<td>MKD</td>
<td>86.0±6.7 (2)</td>
<td>88.0±6.2 (2)</td>
<td>52.0±57.2 (3)</td>
<td>14.0±28.2 (2)</td>
<td>77.3±28.4 (3)</td>
</tr>
<tr>
<td>MKT-A</td>
<td>88.3±6.2 (4)</td>
<td>88.8±22.2 (4)</td>
<td>33.8±26.4 (4)</td>
<td>36.5±26.3 (4)</td>
<td>72.8±11.0 (4)</td>
</tr>
<tr>
<td>MKT-B</td>
<td>91.0±4.6 (4)</td>
<td>91.5±2.4 (4)</td>
<td>27.0±11.5 (4)</td>
<td>26.0±11.7 (4)</td>
<td>66.3±10.1 (4)</td>
</tr>
</tbody>
</table>

p value: 0.92 0.25 0.45 0.53

Although not significant, we observed treatment-related trends in physiologic parameters (Table 2). Percent oxygen saturation of hemoglobin was low to within acceptable ranges for all treatment groups (Table 2). Kreeger et al. (2002) noted the lack of data on the physiological effects of SpO₂ < 90 and felt the trend was more important. All time points where data was available showed an increase in value and lower variability in SpO₂ at 40 min compared to 20 min. Kreeger et al. (2002) considered body temperatures > 40°C to represent a state of hyperthermia. Elevated body temperatures were recorded in all treatments groups except the MKT-B. Temperatures were sufficiently elevated to require administration of cold-water enemas in two of three XK, two of three MKB and one of four MKB treated deer during the trials. Maximum ambient temperature for Athens, Georgia for each day during our trials was 26, 24 and 18°C (NOAA National Climatic Data Center, http://cdl.noaa.gov/ulck/ULC/ULC). Because we intervened to lower potentially dangerous body temperatures of some deer, statistical comparisons of post-treatment temperatures were not valid. One previously hyperthermic doe receiving MKB was found dead in the outer pens on 2 May 2005, approximately 3 weeks post drug trial. She appeared healthy the day after treatment. No necropsy was performed due to advanced decomposition of the carcass.

There were no differences among treatments for time to head up and standing after antagonist administration (Table 1). However, two of the three XK deer were reversed early because of hyperthermia. The third XK deer was not approachable and thus not given the antagonist. In the MKB group, two of three deer were reversed early because of hyperthermia. We recorded sedation scores for MK, MKT-A and MKT-B treatments and found no significant differences among these treatments at any point (Fig. 1); however MKT-B qualitatively showed a rapid and predictable reduction in sedation.

Fig. 1: Mean sedation scores of captive white-tailed does after treatment with selected immobilizing drugs and corresponding antagonists, 11-13 April 2005, Athens, Georgia. Deer were given the antagonist (0.35 mg kg⁻¹ atipamezole) 45 min after lateral recumbency. Sedation score of 5 = lateral recumbency with no sign of reversal. Sedation score of 0 = no sign of sedation. There were no differences among drug treatments at any point.

MK = 0.075 mg kg⁻¹ Medetomidine and 2.1 mg kg⁻¹ Ketamine, MKT-A = 0.063 mg kg⁻¹ Medetomidine, 0.9 mg kg⁻¹ Ketamine and 2.0 mg kg⁻¹ tiletamine/zolazepam, MKT-B = 0.067 mg kg⁻¹ Medetomidine, 1.4 mg kg⁻¹ ketamine and 1.1 mg kg⁻¹ Tiletamine/zolazepam.

Because of our daily monitoring of females during the fawning season, we documented neonatal health problems in fawns born to five of 18 treated does. However, one of seven untreated does had an unhealthy fawn as well. The fawns were either stillborn or unthrifty at birth. We were not able to determine if the neonatal health problems were drug or handling related.

**DISCUSSION**

All treatments except XK effectively immobilized the deer. However, our MK dose did not induce a deep level
of anesthesia. Satisfactory immobilization using a higher dose of MK in mule deer (O. hemionus) and mule/white-tailed deer hybrid (0.1 mg kg\(^{-1}\) medetomidine and 2.5 mg kg\(^{-1}\) ketamine) was found (Caulkett et al., 2000). In our study, the addition of butorphanol potentiated the anesthetic effect of MK. However, we do not recommend MKB because of the potential for hyperthermia possibly due to the excitable induction and the high cost of antagonists for this combination. Other opioids have been associated with hyperthermia in white-tailed deer (Miller et al., 2003; Caulkett et al., 2000). The MKB deer that was found dead 3 weeks after the drug trial, was clinically normal prior to its death but exhibited hyperthermia at treatment.

Qualitatively, MKT-A and MKT-B were both effective and relatively safe for chemically immobilizing pregnant deer with sternal recumbency occurring at 4.7+1.0 and 4.6+1.1 min, respectively. Previous research found that mean time to sternal recumbency was 2.4+0.7 for adult female deer treated with xylazine (2.2+0.2 mg kg\(^{-1}\)) and tiletamine-zolazepam (4.5+0.4 mg kg\(^{-1}\)) (Miller et al., 2004). Although shorter induction times occurred with their xylazine and tiletamine-zolazepam combination, recovery times were extensive. Times to sternal and lateral recumbency are important factors in determining flight distances of deer after darting them in field situations. However, recovery time also is critical when releasing these deer post-capture. Partially anesthetized may experience increased predation, intraspecific strife and accidents. Additionally, there is concern for public safety in urban/suburban areas (e.g., deer-vehicle collisions). Therefore, not only induction time, but also recovery time should be considered when deciding on drug protocols for darting deer. The MKT-B group was quickly reversed to minimal sedation after the antagonist was given. Sedation scores of MKT-B were less than MKT-A at 1-2 h after antagonist administration (Fig. 1).

Calculated costs for drug treatment were similar for MK, MKT-A and MKT-B (Table 3). The cost of MKB was increased greatly by the additional cost of the antagonist, naltrexone. Although XK cost only $4.86 per dose, it was not effective in immobilizing the deer.

In addition to effectiveness and cost, safety must be a primary consideration. Both MKT-A and MKT-B provided acceptable physiological parameters (Table 2). However, there appeared to be problems with neonatal survival. We do not know whether these problems were due to drug treatments or late-gestation handling stress. DelGiudice et al. (1986) found no adverse effects on pregnancy or differences in neonatal survival in does repeatedly given XK during gestation compared to non-immobilized does. Xylazine has been shown to decrease uterine blood flow in pregnant cows (Hodgson et al., 2002). This reduction in flow could potentially result in calf morbidity and/or mortality. At this time, we do not recommend chemically immobilizing late-term pregnant does with our drug protocols.

**CONCLUSION**

The combination of ketamine (for a relatively shorter recovery time), tiletamine-zolazepam (for rapid induction) and medetomidine (for synergistic effects and increased relaxation) may provide a superior immobilization regimen in white-tailed deer. This study provided preliminary data on the effective and safe use of MKT-A and MKT-B for chemically immobilizing captive deer. Future research should evaluate these drug combinations administered by darting in wild deer.

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