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IMMOBILIZATION OF MULE DEER WITH THIAFENTANIL (A-3080) OR THIAFENTANIL PLUS XYLAZINE

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ABSTRACT: We evaluated thiafentanil oxalate (A-3080) for the immobilization of mule deer (*Odocoileus hemionus*) under laboratory and field conditions. In a crossover experiment comparing recommended (0.1 mg/kg) and 2× recommended thiafentanil doses in captive deer, both produced rapid induction and immobilization. Mean induction was shorter ($P=0.013$) for the 2× group (1.9 vs. 3 min); mean reversals for both groups were rapid (recommended=0.9 min after naltrexone injection; 2×=1 min) and did not differ ($P=0.29$). Six free-ranging mule deer were immobilized with 7 mg thiafentanil and four with 10 mg; mean induction was 2.3 min for both groups (95% confidence interval [CI]: 7 mg, 1.2–3.4; 10 mg, 1.9–2.8), and mean reversal was <1 min for both groups. Of 165 free-ranging deer darted with various combinations of thiafentanil and xylazine, we successfully immobilized 148 (90%). Mean induction ranged from 2.1 to 4.9 min for different drug combinations. Reversals were not compared because naltrexone and yohimbine doses varied, but overall mean reversal was 1.9 min (95% CI, 1.7–2.1 min) after injection of naltrexone and yohimbine intravenously (IV); naltrexone:thiafentanil ratios ranging from 10:1 to 43:1 provided mean recoveries ranging from 1.5 to 2.3 min. All 25 deer fitted with radio collars were alive at 30 days postcapture. On the basis of overall reliability and effectiveness, drug volumes, and ease of handling drugged animals, we recommend using a combination of 10–12 mg thiafentanil (0.15–0.2 mg/kg) and 100 mg xylazine to immobilize mule deer; immobilization can be effectively reversed with 100 mg naltrexone or more and 15 mg yohimbine or more IV. Where feasible, we also recommend the use of transmitter darts when immobilizing mule deer with opioids in order to maximize recovery of darted deer and to ensure that missed darts are found.

Key words: A-3080, chemical immobilization, Colorado, mule deer, naltrexone, *Odocoileus hemionus*, opioid narcotics, thiafentanil, xylazine.

INTRODUCTION

Synthetic opioids are widely used for capturing wild ungulates. Opioids like etorphine (M99) and carfentanil have been particularly valuable in wildlife work because they provide rapid induction and relatively long-lasting immobilization and because their effects can be reversed with specific opioid antagonists (Thorne, 1982; Allen et al., 1991). New analogs continue to be developed and made available for wildlife applications and might offer advantages over existing compounds in some species (Lance, 1991).

Thiafentanil oxalate (A-3080), a highly potent opioid anesthetic, has been used in Rocky Mountain elk (*Cervus elaphus nelsoni*; Stanley et al., 1988a), impala (*Aepyceros melampus*; Janssen et al., 1993), and pronghorn (*Antilocapra americana*; Kree-

ger et al., 2001). As with carfentanil and the other opioids used in wildlife capture, thiafentanil's effects are quickly antagonized with naltrexone. However, thiafentanil offers two important potential advantages over carfentanil. Compared with carfentanil, thiafentanil has a significantly shorter duration of action but is only slightly less potent (Stanley et al., 1988b; Janssen et al., 1991). Moreover, thiafentanil apparently offers a greater margin of safety than carfentanil: in a domestic ferret (*Mustella putorius furo*) laboratory model, the therapeutic index of thiafentanil was about 4× higher than the therapeutic index for carfentanil (48 vs. 16; Stanley et al., 1988b). Here, we report data from laboratory and field studies evaluating thiafentanil and thiafentanil in combination with xylazine HCl in immobilizing mule deer (*Odocoileus hemionus*).

MATERIALS AND METHODS

In both laboratory and field studies, we evaluated an experimental formulation of thiafentanil oxalate (10 mg/ml, INAD 10-739, Wildlife Pharmaceuticals Inc., Fort Collins, Colorado, USA). In all applications, thiafentanil was antagonized with the use of a commercially available formulation of naltrexone HCl (50 mg/ml) (Trexonil®, Wildlife Pharmaceuticals).

Experimental assessment

For experimental assessment, we used 10 captive adult (>1 yr old) mule deer held at the Colorado Division of Wildlife's Foothills Wildlife Research Facility (Fort Collins, Colorado). All deer were uniquely identified by marked plastic ear tags or collars. Eight of these deer were weighed on a calibrated scale prior to the study; we estimated weights of the other two deer that could not be worked on the scale by visual comparisons to deer of known weight.

Our experiment had a balanced, crossover design. We randomly assigned each deer to one of two thiafentanil dose treatments: one treatment was the study protocol dose (0.1 mg/kg), and the other treatment was 2× the protocol dose (0.2 mg/kg). The latter treatment was used to aid in assessing margin of safety. For both treatments, thiafentanil was antagonized by naltrexone (100 mg/mg thiafentanil). Treatment assignments were switched for the second half of the experiment so that each animal eventually received both treatments. The first half of the crossover was run on day 0, and the second half was run 14 days later. All trials were conducted during October 2001.

Thiafentanil was delivered intramuscularly (IM) via single-use, 1- or 2-ml 13-mm-diameter darts equipped with gel-collared 32-mm-long needles (Pneu-dart, Williamsport, Pennsylvania, USA) shot from a CO₂-powered rifle (DanInject®, Wildlife Pharmaceuticals). We recorded induction (elapsed time from dart placement until deer was recumbent) to the nearest 0.1 min. Once recumbent, the animal was briefly examined, blindfolded, and given 5 ml penicillin suspension (penicillin G benzathine and penicillin G procaine, G.C. Handford Manufacturing Company, Syracuse, New York, USA) to prevent dart site infection. We measured and recorded heart rate, respiration rate, and rectal temperature at 3-min intervals. Animals were reversed 15 min postinduction with the study protocol dose and route of naltrexone (100 mg/mg thiafentanil): 25% of the naltrexone dose was given intravenously (IV) and the other 75% subcutaneously (SC). We recorded recovery (elapsed time from injection of antagonist to when the deer was walking on its own)

to the nearest 0.1 min. Deer were observed daily for adverse side effects for 14 days after each treatment.

Field assessment

To evaluate thiafentanil alone for capturing deer under field conditions, we immobilized 10 free-ranging adult mule deer with 7 mg thiafentanil (six deer) or 10 mg thiafentanil (four deer). Deer weights were estimated by averaging weights from the captive deer study. Thiafentanil was delivered in 1-ml single-use darts (Pneu-dart) via a CO₂-powered rifle (DanInject) as in the laboratory study. Induction was recorded to the nearest 0.1 min. Once recumbent, the animal was examined, blindfolded, and given 5 ml combined penicillin suspension to prevent dart site infection. Each deer was marked with a unique metal ear tag and weighed with a suspended scale. Heart rate, respiration rate, and body temperature were measured at 3-min intervals and recorded. We reversed deer 15 min postinduction with naltrexone; the dose was divided into 100 mg IV and 200–250 mg SC. Recovery was recorded to the nearest 0.1 min.

In conjunction with other field studies (e.g., Wolfe et al., 2002) conducted April 2001 to April 2002, we used thiafentanil in combination with xylazine HCl (100 mg/ml, various sources) for mule deer capture. In these captures, drugs were delivered to free-ranging mule deer in 2-ml single-use darts (Pneu-dart) with 32-mm barbed or gel-collared needles or in 2-ml transmitter darts (Pneu-dart) with 32-mm barbed needles. All darts were fired from a CO₂-powered rifle (Daninject). We used various combinations of thiafentanil and xylazine for capture (Table 1). When feasible, we recorded induction as above. Heart rate, respiration rate, and rectal temperature were measured and recorded at least once during handling. These deer were marked with metal ear tags and either plastic ear tags, a radio collar, or a plastic collar. Thiafentanil immobilization was reversed with naltrexone administered (SQ, IV, or both) as a split dose in most cases. Yohimbine HCl (15–20 mg IV) (Antagonil®, Wildlife Pharmaceuticals) was used to reverse xylazine. Recovery was recorded as above. All deer were monitored for adverse effects during handling procedures, and 25 deer with radio collars also were rechecked 1, 7, and 30 days after capture.

We analyzed experimental data on induction and recovery as well as rectal temperature and vital rates, comparing recommended and 2× dose treatments with the use of paired *t*-tests. For pulse and respiration rates, we compared values at 5.7(±0.3) min after induction; for rec-

TABLE 1. Induction and capture success rates using different thiafentanil:xylazine combinations in mule deer in northeastern Colorado, USA.

| Thiafentanil: xylazine (mg:mg) | Number ^a | Induction (min) (mean, 95% confidence interval) | Successful captures/ attempts ^b | Month of capture |
|--------------------------------------|---------------------|---|--|-----------------------|
| 5:50 | 18 | 2.1 (1.7–2.4) | 21/24 | Apr–May |
| 5:100 | 3 | 4.2 (0.9–7.5) | 5/5 | Jun–Aug |
| 5:150 | 7 | 3.0 (0.8–5.3) | 10/11 | Jun–Sep |
| 7:30 | 8 | 4.9 (2.0–7.9) | 8/9 | May |
| 7:130 | 13 | 3.6 (1.5–5.7) | 19/21 | Sep–Oct |
| 10:100 | 36 | 2.1 (1.7–2.4) | 44/48 | May, Aug–Oct, Jan–Apr |
| 13:70 | 5 | 2.0 (1.6–2.5) | 5/5 | Oct |
| 15:50 | 26 | 2.4 (1.8–3.0) | 30/36 | Oct, Mar |

^a Number of immobilizations in which induction could be measured.

^b All attempts, including those in which immobilization occurred but induction could not be measured. Six additional deer were successfully captured with other combinations of thiafentanil and xylazine, but data are not reported here.

tal temperatures, we compared the highest temperatures measured during immobilization. We used $\alpha=0.05$ to assess statistical significance. For field studies, we had no a priori hypotheses; consequently, we report only means and 95% confidence intervals (CI) on measured times and rates.

RESULTS

Experimental assessment

All 10 captive mule deer were successfully immobilized with either the recommended or 2 \times -recommended thiafentanil doses. Both doses produced rapid induction and immobilization in all animals. Induction was shorter ($P=0.013$) for the 2 \times group (mean \pm SE, 1.9 ± 0.2 min vs. 2.7 ± 0.4 min). Reversals for both groups were rapid (recommended = 0.9 ± 0.1 min; 2 \times = 1 ± 0.1 min) and did not differ ($P=0.29$). Pulse (recommended = 66 ± 8 beats/min; 2 \times = 71 ± 8 beats/min), respiration (recommended = 29 ± 3 breaths/min; 2 \times = 29 ± 2 breaths/min), and maximum rectal temperatures (recommended = 39.5 ± 0.2 C; 2 \times = 39.6 ± 0.3 C) did not differ between dose treatment groups ($P \geq 0.65$). Immobilized deer showed typical opioid-induced muscle rigidity, kicking, odontoprism (grinding teeth), and ptialism (salivation); the combination of grinding and salivation often produced frothing around the mouth. None of the deer showed signs of renarcotization or adverse side effects during posttreatment obser-

ations. Three animals became hyperthermic (rectal temperatures >40.6 C) while immobilized, and one of these was recovered early; however, none of the three showed any long-term adverse effects.

Field assessment

Of the 10 free-ranging mule deer tested (six with 7 mg and four with 10 mg thiafentanil), induction was 2.3 min for both groups (95% CI: 7 mg = 1.2–3.4 min; 10 mg = 1.9–2.8 min). Mean reversal was 0.9 min (95% CI, 0.4–1.3 min) for deer immobilized with 7 mg thiafentanil and 0.6 min (95% CI, 0.02–1.2 min) for deer immobilized with 10 mg thiafentanil.

Of 165 free-ranging deer darted with various combinations of thiafentanil and xylazine, we successfully immobilized 148 (90%); 93 of 100 females and 55 of 65 males were successfully captured. Complete data sets were available for 116 of the free-ranging mule deer immobilized (Table 1); we were unable to accurately measure induction for the remainder. Mean induction for the different drug combinations ranged from 2.1 to 4.9 min (Table 1). All combinations produced immobilization adequate for routine handling and sampling. However, at lower doses of thiafentanil, higher doses of xylazine were required to produce adequate muscle relaxation needed for some procedures, and

in some cases, we gave an additional 50 mg xylazine IV to facilitate sampling.

Comparisons were not made for reversal associated with specific thiafentanil:xylazine combinations because doses of naltrexone and yohimbine varied. Reversal with naltrexone or naltrexone plus yohimbine provided rapid recovery: overall, mean reversal was 1.9 min (95% CI, 1.7–2.1 min). Compared with recoveries from thiafentanil alone, the approximately 1-min delay in mean recovery was likely caused by the presence of xylazine. Naltrexone:thiafentanil ratios ranging from 10:1 to 43:1 provided mean recoveries ranging from 1.5 to 2.3 min.

In general, deer remained stable during immobilization and recovered uneventfully. One animal showed signs of hyperthermia. Among 25 deer that were fitted with radio collars, there was no mortality 30 days or less postcapture. We failed to capture 17 deer (10 males and seven females) with various combinations of thiafentanil and xylazine (Table 1). In two cases in which transmitter darts failed, darted deer were found dead 1 and 2 days later. No cause of death was found on necropsy at the Colorado State Diagnostic Laboratory (Fort Collins, Colorado). In two other cases, darted deer that eluded capture were seen more than 1 hr later and were recovering from the anesthetic. The fates of other deer that eluded capture were not determined.

DISCUSSION

Thiafentanil appears to be an effective drug for immobilizing both captive and free-ranging mule deer. Our primary field study required that free-ranging deer be captured in urban settings. Because many of these deer were being captured in close proximity to houses, roads, and bystanders, we needed an immobilization agent that would provide rapid induction and could be rapidly and completely reversed. Thiafentanil provided adequate immobilization with and without the addition of xylazine in all animals that were captured.

Animals drugged with thiafentanil alone had the muscle rigidity typical of opioid immobilization in ungulates (Kreeger et al., 2002). In contrast to experiences reported for pronghorn (Kreeger et al., 2001), adding xylazine improved muscle relaxation and ease of handling and sampling in mule deer. Compared with immobilization with thiafentanil alone, adding xylazine also greatly reduced ptialism and odontoprisis. In general, we observed that deer immobilized with higher doses of thiafentanil showed less muscle rigidity and were easier to handle and sample. Deer immobilized at lower thiafentanil doses required higher doses of xylazine to establish comparable levels of muscle relaxation.

Reversal with naltrexone or naltrexone plus yohimbine provided rapid recovery. Previous studies of opioid antagonism in wild ungulates have recommended using 100 mg naltrexone/mg opioid given (Miller et al., 1996; Kreeger et al., 2001), with the dose divided between IV and IM or SC routes. Although this regimen produced rapid recovery from thiafentanil immobilization in both captive and free-ranging deer, we also observed excellent recovery (1.2–2.6 min) with IV naltrexone doses as low as 100 mg ($n=31$). Naltrexone:thiafentanil ratios ranging from 10:1 to 43:1 provided rapid recoveries (1.5–2.3 min), suggesting that lower naltrexone doses are sufficient to antagonize thiafentanil immobilization in mule deer. Renarcotization was not observed in any of the deer. Although we did not have opportunities to explicitly reevaluate free-ranging deer for renarcotization, many were captured in urban areas where deer displaying signs of renarcotization would have been reported. Moreover, we have not observed renarcotization after use of low-dose naltrexone in captive mule deer immobilized subsequent to this study (L. L. Wolfe, unpubl. data).

Aside from muscle rigidity, which was managed by the addition of xylazine, the most common problems encountered

were hyperthermia and failure to capture. However, we observed no other short- or long-term adverse effects even at twice the original recommended dose. Hyperthermia was rare (1 of 148 cases) in captured deer when thiafentanil was used in combination with xylazine. In the experimental assessment of thiafentanil alone, two of the three deer that became hyperthermic were excited and running before being darted. For the use of thiafentanil alone, we recommend caution when darting excited animals and in high ambient temperatures to avoid hyperthermia.

Deer that eluded capture appeared to exhibit excitatory behavior and started running 1–2 min after being darted. Some of these animals might have been underdosed because of poor dart placement or incomplete injections. Despite exhaustive searches for downed animals, we were unable to locate deer, either because of the distances that they ran or thick cover. The two animals that were found dead were both darted in August, but necropsy results were inconclusive. Stanley et al. (1988a) reported recovery from thiafentanil immobilization in elk without antagonist; unassisted recovery also was observed in two mule deer from our field study. Among excitatory deer that we were able to track with transmitter darts, they often stopped running after becoming entangled in thick brush or encountering a solid object such as a fence or trailer. Similar observations were made in impala immobilized with thiafentanil (Janssen et al., 1993). Kilpatrick et al. (1997) reported a comparable (86%) recovery rate in deer darted with a ketamine:xylazine combination by transmitter darts; they concluded that capture failures were a result of poor shot placement, incomplete injection of drugs, or transmitter failure. On the basis of our experiences, we recommend the use of transmitter darts when darting deer with opioids to increase the likelihood both of finding animals that might manifest excitatory behavior and of retrieving missed darts. Our recommendation is tem-

pered by experiences in which accurate darting in windy conditions or at long distances with transmitter darts was substantially compromised by the length and weight of the darts. Barbed transmitter darts also were more traumatic to deer than standard gel collar darts and could have contributed to darted deer running away in some cases.

On the basis of our field observations, overall reliability and effectiveness, drug volumes, and ease of handling drugged animals, we recommend the use of a combination of 10–12 mg thiafentanil (0.15–0.2 mg/kg) and 100 mg xylazine to immobilize mule deer in situations in which rapid immobilization and recovery are needed. Immobilization produced by this thiafentanil:xylazine combination can be effectively reversed with 100 mg naltrexone or more and 15 mg yohimbine or more (both delivered IV).

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