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USING TAILORED TRANQUILIZER COMBINATIONS TO REDUCE STRESS ASSOCIATED WITH LARGE UNGULATE CAPTURE AND TRANSLOCATION

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ABSTRACT: Capture and translocation are important tools for managing and studying large ungulates. Although widely used, many established field practices cause fear and stress in subject animals that can hamper overall effectiveness and safety. Over the last 10 years we have been exploring uses of tranquilizer combinations as adjuncts to wild ungulate capture and translocation work in Colorado, USA. Our approaches have been tailored to various field applications to reduce fear and stress, facilitate handling, and improve the overall success of capture and translocation for research or management purposes. For physical capture (drop net or helicopter-net gunning) with local release, combinations of midazolam and azaperone administered immediately upon capture provide transient tranquilization and muscle relaxation during manual restraint and handling to prevent hyperthermia and capture myopathy. For extended tranquilization (during transport and overnight holding), adding a sustained-release haloperidol formulation provides calming effects for at least 24–48 h. In our assessment, appropriate and adaptive use of these tranquilizer combinations benefits captured animals without impeding management or research goals

Key words: Animal welfare, azaperone tartrate, benzodiazepine, butyrophenone, capture, haloperidol, midazolam HCl, stress.

INTRODUCTION

Capture is an important tool for managing and studying wildlife. Although done largely to benefit populations or species, capture may be detrimental to those individuals being handled. For most nondomesticated animals, being subdued by an individual of a different species is a prelude to death. Consequently, capture and handling likely cause extreme distress and fear in wild individuals (Spraker 1982; Ebedes and Raath 1999; McLaren et al. 2007). In this context, we have sought ways of minimizing unintended adverse effects of capture and handling in the wild ungulate species routinely captured and handled by Colorado Division of Parks and Wildlife (CPW) field personnel, following the lead of pioneering work done in southern Africa (reviewed by Ebedes and Raath 1999).

The adverse collateral physiological effects of capture on wild ungulates have long been recognized (Spraker 1982; Ebedes and Raath 1999; Paterson 2007). Attempts to treat hyperthermia and capture myopathy, two common consequences of wild ungulate capture and translocation, are often both fruitless and frustrating (Paterson 2007; Kreeger and Arnemo 2012). In our experience, medical intervention for capture myopathy rarely proves effective because treatment needs to begin before tissue damage (e.g., rhabdomyolysis) occurs. Although hyperthermia can be mitigated in some cases, this often arises as a result of prolonged pursuit and manual restraint that also precipitates rhabdomyolysis; moreover, the long-term effects manifest as organ damage and seem likely to be underestimated in released animals.

Beyond the physical and physiological effects, capture and translocation likely take psychological and social tolls on subject animals (Spraker 1982; Ebedes and Raath 1999; McLaren et al. 2007). Capture and handling are undoubtedly stressful for wildlife, but novel environment is also a potent stressor even for domestic animals (Keeling and Gonyou 2001; Möstl et al. 2002). It follows that translocation causes sustained fear

and stress in wild animals (Ebedes and Raath 1999; Read and McCorkell 2002; McLaren et al. 2007). Such effects may be compounded when social bonds become disrupted (Keeling and Gonyou 2001) as a result of capture or relocation. Given the relative ineffectiveness of medical intervention in addressing capture-related health problems, emphasis has shifted to preventive medicine.

Wildlife capture and handling undertaken by CPW began to improve when preventive measures within our control, such as reducing or limiting pursuit and handling times and avoiding or working around extreme ambient temperatures and snow depth, were institutionalized. The use of drugs to reduce fear and anxiety (Ebedes and Raath 1999) further improved handling, transport, and animal care as described below. Chemical immobilization drugs, although safe and effective for capture, were not considered appropriate for animals left unattended for transport in a sling under a helicopter or in a trailer. Our goal was to reduce fear, anxiety, muscle tension, and struggling, but to leave the animal awake enough to stay upright, swallow, and keep its airway open. The duration of drug effects needed to be sufficiently short acting for release after handling and sampling in some situations or sufficiently long acting to hold animals overnight or longer for transport in others. In addition to field applications, we recognized that some of these drugs could be useful in captive research for introducing animals to new enclosures and mixing groups of animals, as well as facilitating sampling and handling (e.g., Ebedes and Raath 1999; Read and McCorkell 2002).

To cover the range of wildlife capture and translocation activities pursued by our agency, we explored uses for combinations of butyrophenone tranquilizers to alleviate fear and stress and benzodiazepine tranquilizers to provide more immediate muscle relaxation without complete sedation. The butyrophenones are antipsychotic drugs that block the action of dopamine, leading to "behavioral quieting" and producing "ataraxia: a state of decreased emotional arousal and relative indifference to stressful situations" (Crowell-Davis and Murray 2006). Butyrophenones produce less sedation and fewer anticholinergic effects than other neuroleptics but can have a higher incidence of extrapyramidal side effects (Ebedes and Raath 1999; Crowell-Davis and Murray 2006). Butyrophenone tranquilizers have been used in a variety of wildlife species (e.g., Colly 1992; Ebedes 1992; Diverio et al. 1993; Ebedes and Raath 1999; Read and McCorkell 2002) The benzodiazepine tranquilizers bind to specific gamma-aminobutyric acid receptors in the central nervous system, acting relatively rapidly to relieve anxiety or fear (Crowell-Davis and Murray 2006). Benzodiazepine tranquilizers have been used alone or in combination with more potent immobilizing agents for capturing and handling a variety of wildlife species (Kreeger and Arnemo 2012).

Two butyrophenones, azaperone and haloperidol, and the benzodiazepine midazolam offered complementary effects, onsets, and durations that met our range of field needs. Azaperone, a relatively short-acting (6–8 h) butyrophenone, has been used in a variety of African wildlife species (Colly 1992; Ebedes and Raath 1999). In North America, azaperone is most widely used in combination with butorphanol and medetomidine (Wolfe et al. 2008, 2014) for wildlife immobilization. We chose compounded azaperone tartrate (Wildlife Pharmaceuticals/ZooPharm, Inc., Windsor, Colorado, USA) for field applications based on onset of action, duration, and availability in a 50 mg/mL concentration. Haloperidol, a longer-acting (>24 h) butyrophenone, acts as both sedative and antipsychotic (Ebedes and Raath 1999; Crowell-Davis and Murray 2006). Haloperidol has been used to desired effect in various African herbivores at dosages ranging from 5 to 60 mg intramuscularly (IM; Ebedes and Raath 1999). We used a sustained-release haloperidol compound (Haloperidol SR, compounded in limited supply, 20 mg/mL, Wildlife Pharmaceuticals,

Inc., Windsor, Colorado, USA) with effects lasting up to 72 h (L.L.W unpubl. data) that was well suited for our specific field needs. (Note: When using the drug combinations we describe, it is important to know whether or not the compounded haloperidol formulation in use is "sustained release" to avoid overdosing.) Midazolam, a short-acting (<2 h) benzodiazepine tranquilizer with minimal respiratory and cardiovascular effects, has an aqueous base and thus has good IM absorption and rapid onset of action (Kreeger and Arnemo 2012). We chose midazolam HCl (Wildlife Pharmaceuticals/ZooPharm, Inc.) compounded at a 50 mg/mL concentration.

Here, we overview cases using azaperone, sustained-release haloperidol, and midazolam in various combinations during capture and sampling of mule deer (*Odocoileus hemionus*), and during moose (*Alces alces*) and bighorn sheep (*Ovis canadensis*) translocations. These case reports illustrate how we tailored the drug combinations to help offset adverse capture-related effects while still meeting specific research or management needs. Our approach for using these three drugs as adjuncts to capture and handling was generally as follows: For animals that were captured and released on site we used a combination of azaperone and midazolam. Animals that were translocated also received a sustained-release haloperidol formulation (as available). Dosing was adjusted "to effect" based on real-time assessments and thus doses are sometimes reported as ranges. Our subjective field assessments were not conducted as formal studies or experiments, but rather represent observations made in the course of assisting managers and researchers and the wild animals they were handling.

EXAMPLE APPLICATIONS

Mule deer capture for sampling and release from a central processing site

As part of a field study conducted during 2010–2014 (Geremia 2014), mule deer were captured with a net gun after professional helicopter pursuit (Quicksilver Air Inc., Peyton, Colorado, USA); pursuit times were limited to <5 min/group and <2 min/individual. Netted deer (mostly adult females weighing about 70 kg) were hobbled, blindfolded, bagged, and transported on long-line slings to a central processing site <5 km away. To reduce stress and improve the ease and safety of deer handling, the capture crew administered 15 mg azaperone (Wildlife Pharmaceuticals, Fort Collins, CO, USA) by IM injection immediately upon capture or when the deer arrived at the processing site, and we also administered 10–15 mg midazolam (Wildlife Pharmaceuticals) by intravenous (IV) injection upon arrival at the processing site. Supplemental oxygen was delivered by intranasal insufflation. Animals were then bled, radio collared, and ultrasounded for body condition and had rectal biopsies taken for prion disease screening. After 15–20 min of processing, deer were released on site. Deer remained calm and relatively relaxed throughout processing; mean $\pm$ 95% confidence interval vitals were temperature 39 ± 0.1 C, heart rate 118 ± 5/min, respiration rate 35 ± 3/min, and blood lactate 9.3 ± 0.7 mmol/L. Released deer showed some residual sedation (e.g., transient incoordination, calm demeanor) but were ambulatory and responsive to human approach. Of 142 deer treated with tranquilizers upon capture, there was only one known death (attributed to clinical prion disease) within 2 wk of release; thereafter, observed survival of these deer approximated rates measured in other field studies using similar capture methods but without tranquilizers (Colorado Division of Parks and Wildlife [C.P.W.] unpubl. data).

In the course of over 400 subsequent mule deer captures done in conjunction with other projects, administering 15 mg azaperone and 35 mg midazolam by IM injection immediately upon capture subjectively appeared more effective for relaxing and calming deer for helicopter transport and subsequent

handling and sampling—probably because midazolam effects came earlier in the handling process—yet still allowed ample time for these animals to metabolize drugs prior to release. Azaperone inadvertently administered without midazolam occasionally caused apparent agitation in mule deer under these capture conditions. We have continued using azaperone (15 mg IM) and midazolam (35–45 mg IM to effect, depending on animal and capture conditions) in mule deer captured for field studies throughout Colorado. In our assessment this practice, combined with pursuit time limits and other preventive measures, appears to have reduced signs of fear and distress (e.g., increased depth of respiration, decreased struggling) in captured individuals compared to earlier practices. Intranasal midazolam could be evaluated as a further potential refinement of this approach.

Moose capture and translocation

In winter 2009 and 2010, 39 moose (adults and juveniles of both sexes) were captured via helicopter-net gunning for translocation to establish a new population in Colorado (Table 1). To reduce stress associated with capture, handling, and trailer transport we treated 37/39 moose with azaperone (40–45 mg IM/adult or 15–25 mg/juvenile) immediately upon capture. As available, we also administered sustained-release haloperidol (30–60 mg IM/adult; Table 1). In the second year, we added IV midazolam (50–100 mg/adult or 15–25 mg/juvenile, titrated to effect) when the animals arrived at the processing site to provide transient sedation and facilitate handling and transferring moose into trailers. Although midazolam could have been administered IM upon capture, we elected to reduce the dose and duration of activity by giving midazolam IV upon arrival for processing. The addition of midazolam aided in short-term tranquilization and facilitated safer handling of moose within the confines of a closed trailer. In some individuals, however, higher midazolam doses caused more pronounced transient sedation that resulted in lateral recumbency, requiring monitoring for about 20 min until affected individuals were able to maintain sternal positioning.

Past translocations of moose had resulted in some capture myopathy (5–10%) and abandonment of at-heel juveniles (>75%) upon release in unfamiliar habitat (Olterman et al. 1994; C.P.W., unpubl. data). The purpose of the azaperone and sustained-release haloperidol was to relieve fear and anxiety during trailer confinement and transport and upon release into a novel environment. We regarded these effects as potentially beneficial in preserving female-juvenile pair bonds after release. All released individuals survived. Moreover, based on visual observations of the released females (all radio marked) no juveniles were abandoned even several months after release. Because we were trying to maximize translocation success there were no controls and thus we cannot say with certainty that the observed outcome was entirely due to the drugs, but the use of long-acting tranquilizers had no appreciable negative effects on postrelease survival under these conditions.

Ground capture of bighorn sheep for translocation

In winter 2010, 12 bighorn sheep were immobilized over a 2-day period via ground darting for translocation using a combination of 30 mg butorphanol, 15 mg azaperone, and 10 mg medetomidine (BAM; Wildlife Pharmaceuticals/ZooPharm, Inc.). The BAM combination provided a small-volume alternative to potent opioids, and an advantage of BAM in this situation was that immobilization could be antagonized while still providing short-term tranquilization from azaperone (Wolfe et al. 2014; L.L.W. unpubl. data). After loading immobilized bighorns into a trailer, we antagonized medetomidine with atipamezole (50 mg IM) and administered 30 mg sustained-release haloperidol IM. The first group of eight bighorns was transported and released into a novel habitat within 4–6 h of capture.

TABLE 1. Combinations of azaperone tartrate, midazolam HCl, and sustained-release haloperidol used in moose (*Alces alces*) and bighorn sheep (*Ovis canadensis*) translocations in Colorado, USA. See text for background, rationale for use, and details. Note that the haloperidol doses listed are for a compounded "sustained-release" formulation.

							Tranquilizer dose in mg (No. treated)		
Species	Capture method	Year	Release site	Age (yr)	Sex	No.	Azaperone	Midazolam	Sustained-release haloperidol[a]
Moose	Helicopter	2009–2010	Flat Tops	>1	Female	21	40–45 (21)	50–100 (10)	30–60 (8)
				>1	Male	8	40–45 (8)	50–75 (4)	60 (3)
				<1	Mixed	10	15–25 (8)	15–25 (6)	nd[b]
Bighorn sheep	Ground dart	2010	Hayman	>1	Mixed	12	15 (19)[c]	nd[d]	10–30 (19)
		2012	Hayman	>1	Female	8	15 (8)[c]	nd[d]	10–16 (8)
		2013	Trout Creek	>1	Female	8	15 (8)[c]	nd[d]	30 (8)
	Drop net	2013	Captivity	>1	Female	13	15 (8)	40 (13)	30 (8)
	Helicopter	2010	Lower Poudre	>1	Mixed	18	15 (18)	75 (18)	30 (18)
		2011	Middle Dolores	>1	Female	9	15 (9)	35 (9)	16 (9)
				>1	Male	3	15 (3)	35 (3)	20–30 (3)
				<1	Mixed	2	15 (2)	35 (2)	10 (2)
		2013	Sangre de Cristo	>1	Mixed	7	15 (7)	20 (7)	nd
		2013	Table Mountain	>1	Female	6	15 (6)	40 (6)	30 (6)
				<1	Mixed	3	15 (3)	40 (3)	nd
		2014	Badger Creek	>1	Mixed	13	15 (6)	40 (13)	30 (13)
				<1	Mixed	2	15 (2)	40 (2)	nd

[a] In using the doses listed, it is important to know whether or not the compounded haloperidol formulation in use is "sustained release" to avoid overdosing.

[b] nd = Not done.

[c] Azaperone delivered in conjunction with butorphanol and medetomidine for immobilization; see text for details.

[d] Butorphanol was not antagonized, and its effects substituted for those of midazolam in bighorns immobilized with butorphanol and medetomidine.

A second group of four bighorns was darted, treated, transported, and released the following day using the same protocol. The antianxiety effects of azaperone and sustained-release haloperidol appeared beneficial in keeping bighorns from the first group calm (as compared to bighorns observed during past releases where haloperidol was not used); bighorns from the first group remained near the release site, where we reunited them with the second group released a day later. We have used this approach with minor variation for other translocations with similar success (Table 1), including two occasions where we brought small groups of bighorn into research facilities for longer-term holding and study.

Helicopter-net gun capture of bighorn sheep with overnight holding and translocation

Fifteen bighorn sheep were captured via helicopter-net gunning over a 2-day period for translocation. Eight individuals captured in late afternoon were held in a trailer overnight; seven additional individuals were captured the following morning. On the first day of capture, each bighorn received 15 mg azaperone and 40 mg midazolam IM; bighorns captured the second day received 40 mg midazolam but no azaperone. Bighorns were blindfolded, hobbled, placed in a sling, and transported under a helicopter to a central processing site. We collected samples, marked animals, and administered 30 mg sustained-release haloperidol IM to each adult. After 4-h transport to a second processing site near the release site, the animals were awake but calm enough for us to enter the trailer, hobble and blindfold each animal, and then place each in a sling for long-line transport to the release site via helicopter. One death occurred within 2 wk postcapture, and that was associated with head trauma that occurred at the time of capture. In previous translocations using helicopter-net gunning we used as high as 75 mg midazolam IM (Table 1) and, although the releases were successful, we regarded the level of sedation as greater than needed; consequently, we titrated down to the 40-mg dose now recommend for handling bighorns in these situations. Lower-dose intranasal midazolam could be explored as an alternative to IM administration in similar applications.

CONCLUSIONS

The foregoing synopses add North American examples of tranquilizer combinations that can be used to improve individual animal welfare during capture and translocation of wildlife. Drug combinations can be tailored to factors such as species, type of capture, and holding times. In our experience, effective use of drugs such as long-acting butyrophenone tranquilizers and rapidly acting benzodiazepine tranquilizers can reduce fear and stress, social disruption, and the incidence of capture myopathy, as well as help prevent injuries to both handlers and animals.

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