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Efficacy of a Butorphanol, Azaperone, and Medetomidine Combination for Helicopter-based Immobilization of Bison (*Bison bison*)

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ABSTRACT: Decreased access to potent narcotics for wildlife applications has stimulated the need to explore alternative drug combinations for ungulate immobilizations. A combination of butorphanol, azaperone, and medetomidine (BAM) has been used for some ungulate species, but information on its use in bison (*Bison bison*) is limited. We conducted field trials using BAM, in conjunction with atipamezole and naltrexone as antagonists, for reversible field immobilization of bison during ground- and helicopter-based operations. We compared times to induction and recovery, vital rates (rectal temperature and respiration rate), and the quality of induction, immobilization, and recovery between ground- and helicopter-based immobilizations of bison. Overall, 15 of 21 bison were induced with the volume we used (mean±SD=3.4±0.6 mL); two other animals darted from a helicopter required a full second dose, and four others (two darted from the ground and two from a helicopter) required a supplemental partial dose to achieve induction. All immobilizations achieved a sufficient plane of anesthesia to permit minor invasive procedures (e.g., skin biopsy and blood sampling). All animals recovered, and most (17 of 21) were reversed in ≤5 min. The mean time to induction was 10.8±7.3 min while that for recovery was 5.0±2.1 min. We found few differences in vital rates or the quality of immobilizations between ground- and helicopter-based captures. The drug combination provided good immobilization and was reliably reversed; however, inconsistent inductions at the doses we used may limit its use in field immobilizations of bison, particularly those animals being darted from a helicopter.

Key words: Aerial darting, BAM, bison, chemical immobilization, ungulate capture.

Carfentanil-based mixtures have been commonly used for field immobilizations of bison (*Bison bison*; Kock and Berger 1987; Haigh and Gates 1995); however, decreased access to potent narcotics for wildlife applications has heightened the need to explore potential alternatives (Lian et al. 2016; Mathieu et al. 2017; Wolfe et al. 2017). Combinations of medetomidine, zolazepam, and tiletamine (MZT), xylazine, zolazepam, and tiletamine (XZT; Caulkett et al. 2000), nalbuphine, medetomidine, and azaperone (NMA; Wolfe et al. 2017), and butorphanol, azaperone, and medetomidine (BAM; T.K. Shury unpubl. data) have all been examined as possible alternative combinations for bison immobilizations. While previous studies have advanced our knowledge of alternatives, none of them investigated aerial-darting from helicopters, which is a necessary and common means of capturing free-ranging ungulates in northern environments (Harms et al. 2012; Lian et al. 2016). Helicopter-based captures induce overt stress in targeted individuals, which may cause additional challenges during field immobilizations. Thus, we need to know the performance of alternative drug combinations not only in ground-based but also in helicopter-based operations.

We investigated the efficacy of BAM for field immobilization of bison. This drug combination is available as a premixed commercial product, consisting of 27.3 mg/mL butorphanol, 9.1 mg/mL azaperone, and 10.9 mg/mL medetomidine (Wildlife Pharmaceuticals, Fort Collins, Colorado, USA), that has been used on a variety of ungulate species (Siegal-Willott et al. 2009; Wolfe et al. 2014; Lapid and Shilo-Benjamini 2015). Butorphanol is a mixed agonist-antagonist opioid that is less potent than other opioids used for wildlife immobilization, such as carfentanil, but has reduced respiratory and cardiovascular side effects (Wenger et al. 2007). The analgesic and sedative properties of medetomidine, an α2-adrenoceptor agonist, support a smooth induction and muscle relaxation during im-

mobilization. The effects of medetomidine are potentiated by opioids like butorphanol and are antagonized by atipamezole (Wolfe et al. 2017). Azaperone is a short-acting butyrophenone tranquilizer that has anti-anxiety properties and has been used in other combinations for immobilizing wildlife (Wolfe and Miller 2016).

Here we provide an evaluation of BAM, in conjunction with atipamezole and naltrexone as antagonists, for reversible field immobilization of bison. We compare times to induction and recovery, vital rates (rectal temperatures and respiration rates), and depths of immobilization among ground-based and helicopter-based captures. We predicted that induction times and vital rates would be higher for animals captured from a helicopter compared to those captured from the ground because of the overt stress induced by being pursued by a helicopter.

We performed ground- and helicopter-based trials of BAM on captive and free-ranging bison, respectively (Table 1). Captive bison were housed in an enclosure at the Yukon Wildlife Preserve (60°43′N, 135°03′W) and immobilized to place ear-tags and administer routine vaccines and antiparasite medication. Animals were not fasted before immobilization. Free-ranging bison had been reintroduced to southwestern Yukon in 1988–1993 (Jung et al. 2015) and were captured primarily to attach GPS collars for management-related research (Jung and Kuba 2015).

All bison were immobilized with BAM. Total drug volumes administered (Table 1) were determined based on information provided by the manufacturer and our experience with BAM for other ungulates. Between November 2016 and January 2017, captive bison were darted from the ground in the upper hindquarter using a carbon dioxide gas-powered rifle (JM Special, Dan-Inject, Bøerkop, Denmark) with 3- or 5-mL Pneu-Dart darts with 40-mm needles (Pneu-Dart Inc., Williamsport, Pennsylvania, USA). Ground-based immobilizations occurred prior to those from a helicopter, allowing us to gain familiarity with the performance of BAM in bison before we attempted helicopter-based immobilizations. During March and July 2017, free-ranging bison were darted from a helicopter in the upper hindquarter using a Dan-Inject rifle (IM model) with 4-mL Pneu-dart darts. To prevent hypoxemia, supplemental oxygen (8–10 L/min) was administered intranasally from a portable oxygen cylinder throughout all immobilizations (Lian et al. 2016; Wolfe et al. 2017). Age was known for captive bison; for those captured by helicopter we estimated age by tooth eruption and annuli on horns (±3 yr; Fuller 1959). Mass (±50 kg) and body condition (scaled from 1–5; Table 1) of immobilized animals was estimated visually by two or three experienced observers.

Induction was measured (±1 min) both from darting to onset of signs (ataxia) and from darting to recumbency. Once sedated, bison were blindfolded and vital rates were measured at the onset of handling and approximately every 5 min during the immobilization. Each animal was scored on a scale of 1–5 based on the quality of the immobilization at each stage (induction, immobilization, and recovery), as defined in Table 2. Antagonists were administered intramuscularly by hand injection at a dose of 4.6 mg atipamezole/mg of medetomidine and 1 mg naltrexone/mg of butorphanol. Recovery was measured (±1 min) from administration of the antagonist to the animal 1) raising its head, and 2) standing and ambulating.

Differences in mean event times (induction, handling, and recovery) between ground-based and helicopter-based immobilizations were assessed with pairwise *t*-tests. We used a general linear model to test the main treatment effects of GROUP (ground-based vs. helicopter-based captures) and TIME (onset vs. end of handling) and their interaction (GROUP*TIME) on vital rates and immobilization quality scores.

We immobilized 21 bison using a mean of 3.4±0.6 mL of BAM per animal (range=2.0–5.0). Mean chase times for darting were 5.0±7.1 min from the ground and 1.3±0.2 min from the helicopter. Overall, two animals darted by helicopter required a full second dose delivered remotely by dart, and four others (two ground- and two helicopter-

TABLE 1. Sample sizes and mean±SD (range) age, estimated mass, body condition score, volume of butorphanol, azaperone, and medetomidine (BAM) administered (see footnote), and estimated volume of BAM for ground- and helicopter-based captures of bison (*Bison bison*) in southwestern Yukon, Canada.

	Ground-based captures				Helicopter-based captures	
	Female (n=7)		Male (n=2)		Female (n=12)	
Parameter	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Estimated age (yr)	6.9±4.5	2–12	11.5±0.7	11–12	5.6±4.1	2–15
Estimated mass (kg)	485.7±70.7	300–600	750.0±70.7	700–800	511.7±124.3	300–600
Body condition score (1–5)[a]	3.6±0.5	3–4	3.4±0.7	3–4	2.4±0.5	2–3
BAM – administered (mL)[b,c]	3.2±0.4	3.0–4.5	4.8±0.4	4.0–5.0	4.3±1.4	3.5–7.0
BAM – estimated volume (mL/100 kg)[b]	0.71±0.21	0.5–1.0	0.64±0.1	0.6–0.7	0.90±0.4	0.6–1.8

[a] Qualitative score (1–5): 1 = emaciated; 2 = thin; 3 = normal; 4 = fat; 5 = very fat.

[b] Values include supplemental volumes (range=0.5–3.5 mL) of BAM administered to achieve induction (n=4 during helicopter captures, n=2 [females] during ground captures).

[c] BAM was premixed at a concentration of 27.3 mg/mL butorphanol, 9.1 mg/mL azaperone, and 10.9 mg/mL medetomidine.

based) required a partial dose hand-injected with a syringe to achieve induction. All animals were ultimately induced, and all immobilizations permitted minor invasive (e.g., skin biopsy and blood sampling) procedures. All animals recovered well, and most (17 of 21) were reversed in ≤5 min. The mean time from darting to induction was 8.7±5.5 min, mean handling time was 34.2±8.9 min, and mean recovery time was 4.9±2.8 min.

The mean drug volume for nine ground-based and 12 helicopter-based bison immobilizations was 3.3±0.9 and 3.5±0, respectively; however, two bison captured from the ground, and four bison captured by helicopter, required a supplemental dose to achieve complete induction (Table 1). We found no significant differences in the mean event times between animals darted from the ground or from a helicopter (P≥0.080; Table 3), but there was much variation in event times among animals in both groups. Medians of our quality scores for induction, immobilization, and recovery were the same for both

TABLE 2. Number, sample size, and median±SD of bison (*Bison bison*) for each quality score ranking (1–5) for the induction, immobilization, and recovery phases of immobilization of bison using BAM during ground- (n=9) and helicopter-based (n=12) captures in Yukon, Canada. Quality scores were scaled from 1–5, with 1 = poorest performance and 5 = best performance (see footnotes for details).

	Ground-based captures			Helicopter-based captures		
Quality score	Induction[a]	Immobilization[b]	Recovery[c]	Induction[a]	Immobilization[b]	Recovery[c]
1	0	0	0	2	0	0
2	2	1	0	2	1	0
3	2	3	0	1	2	2
4	3	5	2	4	9	0
5	2	0	7	3	0	10
n	9	9	9	12	12	12
Median	4±1.1	4±1.0	5±0.4	4±1.5	4±0.7	5±0.8

[a] 1 = no sign of induction, received a subsequent full dose; 2 = recumbent but required a partial dose to remain down or for safe handling; 3 = induction took >10 min after drug administration; 4 = induction took 6–10 min; 5 = induction in ≤5 min.

[b] 1 = recumbent but able to stand with stimulation; 2 = recumbent but easily responsive to stimulation; 3 = recumbent and minimally responsive to stimulation; 4 = good sedation level for sampling and handling; 5 = deep level of sedation.

[c] 1 = animal did not recover; 2 = recovery took >20 min; 3 = recovery in 11–20 min; 4 = recovery in 6–10 min; 5 = recovery in ≤5 min.

TABLE 3. Mean±SD (range) event times (minutes) for field immobilization of bison (*Bison bison*) using butorphanol, azaperone, and medetomidine (BAM) during ground- (n=9) and helicopter-based (n=12) captures in Yukon, Canada. Induction times are from drug administration (in two cases event times are after administration of additional drug with a second dart) until ataxia or recumbency are observed. Handling time is from recumbency to administration of the antagonists. Reversal times are from when the reversal was administered until the animal was able to raise its head or stand up. Test statistics (t and P values) are based on t-tests.

Event times	Ground-based captures	Helicopter-based captures	Test statistics	
			t value	P value
Induction: ataxia	6.2±3.7 (3–15)	5.0±1.8 (3–9)	0.884	0.390
Induction: recumbency	10.8±7.3 (3–26)	7.1±3.2 (3–14)	1.836	0.082
Handling	36.0±8.2 (25–51)	32.8±9.5 (15–49)	0.799	0.434
Reversal: head up	4.2±2.3 (3–10)	3.4±2.8 (1–11)	0.714	0.484
Reversal: stand up	5.0±2.1 (3–10)	4.8±3.6 (2–13)	0.130	0.898

ground-based and helicopter-based captures of bison (Table 2); however, scores for recovery were consistent (4–5) while those for induction were variable (1–5).

Means between vital rates and relaxation scores of bison immobilized from the ground and from a helicopter were similar (Table 4). A general linear model indicated no significant differences between the two groups of bison, or between the time the first and second readings of vital rates were taken, with two exceptions (Table 5). First, relaxation scores were significantly greater over time (Table 4), indicating that animals were in deeper immobilization at the end of the handling period than at the beginning. Second, the interaction term (GROUP*TIME) was significant for rectal temperature, given that it remained similar between the first and last reading for animals darted from a helicopter but it decreased for those darted from the ground (Table 4).

Induction times for bison immobilized with BAM were variable. The BAM mixture immobilized 15 of 21 bison at the applied doses. The other six animals required full or partial supplemental doses to reach induction. The distribution of quality scores reflected the inconsistency we observed in induction times, particularly for bison darted from a helicopter. All animals were sufficiently immobilized to permit routine field procedures (after supple-

TABLE 4. Means±SD (range) vital rates and immobilization quality scores for field immobilization of bison (*Bison bison*) using butorphanol, azaperone, and medetomidine (BAM) during ground- (n=9) and helicopter-based (n=12) captures in Yukon, Canada. Time values at T_1 were taken at the onset of handling while those at T_2 at the conclusion of handling.

	Ground-based captures				Helicopter-based captures			
	T_1		T_2		T_1		T_2	
Response parameter	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Respiration rate (breaths/min)	37.1±19.7	12–68	47.8±17.1	20–66	34.2±9.2	24–54	34.5±9.3	24–48
Rectal temperature (C)	38.3±0.4	38.0–39.0	37.9±0.5	37.4–38.7	39.4±1.3	37.2–41.2	39.4±1.3	37.6–41.2
Immobilization score (1–5[a])	2.7±1.2	1–4	3.3±1.0	1–4	2.8±1.0	2–4	4.0±0	4

[a] 1 = recumbent but able to stand with stimulation; 2 = recumbent but easily responsive to stimulation; 3 = recumbent and minimally responsive to stimulation; 4 = good sedation level for sampling and handling; 5 = deep level of sedation.

TABLE 5. Test results (*F* and *P* values) from general linear models of the difference in means in vital rates and immobilization quality scores between main treatment effects of GROUP (ground-based vs. helicopter-based) and TIME (T_1 vs. T_2), and their interaction (GROUP*TIME), for bison (*Bison bison*) immobilized with BAM in Yukon, Canada. Values at T_1 were taken at the onset of handling while those at T_2 at the conclusion of handling. Model results all with 3,32 degrees freedom.

	Group		Time		GROUP*TIME	
Response parameter	*F* value	*P* value	*F* value	*P* value	*F* value	*P* value
Respiration rate (breaths/min)	0.001	0.996	0.507	0.481	0.146	0.705
Rectal temperature (C)	2.845	0.101	0.895	0.351	4.991	0.032
Immobilization score (1–5)[a]	0.400	0.531	6.947	0.013	0.278	0.602

[a] 1 = recumbent but able to stand with stimulation; 2 = recumbent but easily responsive to stimulation; 3 = recumbent and minimally responsive to stimulation; 4 = good sedation level for sampling and handling; 5 = deep level of sedation.

mental doses in six cases), and reversals with atipamezole and naltrexone were generally smooth, quick, and reliable.

Mean induction times from ground-based immobilizations in our study (10.8±7.3 min) using BAM were lower than those reported in similar studies using an earlier version of BAM (14 min [range=10–18]; T.K. Shury unpubl. data) or NMA (11.5±1.3 min; Wolfe et al. 2017), but greater than that observed for XZT (5.5±1.1 min), MZT (8.8±2.1 min; Caulkett et al. 2000), or a carfentanil-xylazine combination (9.3±1.3 min; Kock and Berger 1987). Our study was only the second to measure the induction time for bison immobilized by helicopter, and our mean induction time (7.1±3.2 min) was slightly higher than that reported for a carfentanil-xylazine combination delivered via aerial-darting (6.5±0.4 min; Haigh and Gates 1995). However, as indicated by the large SD of the means and our quality scores, BAM provided inconsistent inductions at the volumes we used for both ground-based and helicopter-based captures. The mean recovery time in our study (4.9±2.8 min) was comparable to that for bison immobilized with NMA (4.0±1.1; Wolfe et al. 2017) and a carfentanil-xylazine combination (4.1±1.6 min; Kock and Berger 1987), but greater than that using MZT (1.7±0.8 min; Caulkett et al. 2000) and less than that using XZT (11.8±9.7 min; Caulkett et al. 2000).

Contrary to our prediction, we did not find any differences in mean induction or recovery times or in vital rates between ground-based and helicopter-based captures. However, four of 12 bison captured via helicopter required supplemental doses of BAM, and the only animals to have rectal body temperatures ≥40 C were from aerial captures. Thus, animals captured via aerial darting received, on average, 1.1 mL more BAM than did those captured from the ground. A limitation of our study may be that low sample sizes, coupled with high variation within groups, precluded finding statistical significances. Our sample sizes, however, are in line with similar studies of bison (Kock and Berger 1987; Caulkett et al. 2000; Wolfe et al. 2017).

We found that BAM in captive and free-ranging bison provided safe, reversible immobilizations that did not rely on potent opioids. We found that inconsistent and sometimes prolonged induction times occurred, which may limit its use in field immobilizations of bison from a helicopter. However, animals remained in a stable plane of anesthesia with minimal side effects, and reversal of BAM with naltrexone and atipamezole was short and reliable. For immobilization of adult female bison, we recommend using 3.5 mL of pre-mixed BAM (95.6 mg butorphanol, 31.9 mg azaperone, 38.1 mg medetomidine) and 4.6 mg atipamezole/mg of medetomidine and 1 mg naltrexone/mg of butorphanol for reversal of the combination, although higher doses may be necessary for more-consistent helicopter-based captures.

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