IMMOBILIZATION OF MOOSE WITH A-3080 AND REVERSAL WITH NALMEFENE HCl OR NALTREXONE HCl

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ABSTRACT: Sixty-two moose undergoing translocation were chemically immobilized with 10 mg of A-3080 intramuscularly (IM) via dart from a helicopter. The animals were given four different reversal regiments IM, 50 mg or 300 mg of Nalmefene hydrochloride (HCl), or 100 mg or 50 mg of Naltrexone HCl. The mean immobilization time was 3.6 ± 2.0 min. The moose recovered (i.e., were standing) in approximately 2.0 min with each of the reversal regimens. There were no deaths or renarcotization observed.

ALCES VOL. 30 (1994) pp.21-24

Potent opioid analgesics are presently the drugs of choice for chemical immobilization of Shiras moose (*Alces alces shirasii*) (Haigh 1990). Several different opioids have been used, including etorphine hydrochloride (M99®, Lemon Co., Sellersville, PA) (Houston 1969), fentanyl citrate (Janssen Pharmaceutica, New Brunswick, NJ) (Haigh 1977) and carfentanil citrate (Wildnil®, Wildlife Pharmaceuticals Inc., Fort Collins, CO) (Franzmann 1984, Seal 1985) all with varying success. A-3080 (Anesta Corp., Salt Lake City, UT), the newest of these drugs, is a N-aryl-N(4-piperidinyl) amide and has a potency about half that of carfentanil and a shorter duration of action. A-3080 is currently being evaluated for chemical immobilization of elk and moose (Bailey *et al.* 1985, Stanley *et al.* 1988).

The employment of powerful opioids as immobilizing agents requires the use of an opioid antagonist to reverse the drugs actions (Allen 1989). Nalmefene hydrochloride (HCl) (Anesta Corp., Salt Lake City, UT) and Naltrexone HCl (Sigma Chemicals, St. Louis, MO) are the two newest narcotic antagonists being evaluated for narcotic reversal in wildlife (Haigh 1990). They are pure antagonists with a long duration of action (Dixon 1986, Verebey 1976). We evaluated the safety and efficacy of A-3080 immobilization and Nalmefene HCl or Naltrexone HCl for reversal of A-3080 in 62 moose that were undergoing translocation.

MATERIALS AND METHODS

During February 1990 and February 1991, 62 moose were translocated within the State of Utah by the Utah Division of Wildlife Resources. The project involved the use of two helicopters, a chase helicopter and a transport helicopter. The chase helicopter would locate several moose, then return to prepare darts and pickup the dart-gunner. When a subject moose was located for darting, the pilot would make a rapid approach, flying the helicopter just behind the animal (approximately 3 meters from the moose). The dart-gunner would aim for large muscle masses of the hind legs. Once a dart was successfully placed, the helicopter would retreat to a distance that would stress the animal as little as possible, but not lose sight of it. All but three moose were given a total dose of 10 mg of A-3080 delivered by a 3 ml dart using the Paxarms darting system (Paxarms Ltd., Timaru, NZ). Time to immobilization after darting was recorded. Following a successful darting, the chase helicopter radioed the transport helicopter. Upon arrival the sling crew placed a

sling around the animal for transport to a horse trailer. The trailers were arranged with a horse trailer (large enough for two adult moose) adjacent to a flat trailer. The moose was placed on the flat trailer where its respiratory rate and rectal temperature were recorded. The sling was removed from the moose and the animal was slid into the horse trailer on the open sling. The antagonist was given IM and the time to standing was recorded. Moose were antagonized with a total dose of either 300 mg (n = 28) or 50 mg (n = 15) of Nalmefene HCl or 100 mg (n = 6) or 50 mg (n = 10) of Naltrexone HCl given IM. (Three moose were darted twice receiving 20 mg of A-3080 and were reversed with 600 mg of Nalmefene HCl.) When two moose were standing and appeared normal, the trailer would depart for the release site. Upon arrival at the release site the trailer was opened and the animals were released. Moose were observed for varying times after release. A single-factor analysis of variance (ANOVA) was used to determine the differences in standing time between animals receiving Nalmefene and Naltrexone. Alpha = 0.05.

RESULTS

Based on weight estimations in the field, the total dose of 10 mg resulted in a dosing range of 55 ug/kg (from a low of 25 to a high of 80). The mean immobilization time for the 59 moose receiving 10 mg of A-3080 was 3.6 $\pm$ 2.0 min with a range of 9 min. Immobilization and recovery times were not included for the 3 moose darted twice. All immobilized moose were sternally recumbent and tractable upon arrival at the trailer. The mean standing time for the 28 moose that were given 300 mg of Nalmefene HCl was 2.0 $\pm$ 0.6 min after injection of the antagonist while the 10 moose given 50 mg of Naltrexone HCl stood an average of 2.4 $\pm$ 0.6 min after injection of naltrexone (Table 1).

All reversals were rapid and complete with no residual ataxia. There was no statistical difference between the standing times of the two reversal agents ($F(3,55) = 1.25$; $P = 0.300$. The mean respiratory rate and temperature upon arrival at the trailer were 29.2 $\pm$ 3.0 breaths/min (n = 57; range 32) and 39.8 $\pm$ 1.1 C (n = 56; range 5.6 C), respectively. There were no deaths or any indication of renarcotization during the observation period post-translocation.

DISCUSSION

The potent opioid analgesic A-3080 produces immobilization by stimulating the opioid receptors in the central nervous system. It is approximately 63% as potent as carfentanil in elk (Stanley 1988). In moose A-3080 maybe only 50% or less of the potency of carfentanil based on the doses (2.5 to 5.0 mg) of carfentanil used by various investigators (Franzmann 1984, Meuleman *et al.* 1984, Seal 1985). The 10 mg dose of A-3080 requires only a volume of 1 ml which would

Table 1. Summary of immobilization and standing times.

n	Agent	Dose (mg)	Mean Immobilization or Standing Time (min)	Extrema (min)
59	A3080	10	3.6 $\pm$ 2.0	1.0-10.0
28	Nalmefene	300	2.0 $\pm$ 0.6	1.1-4.2
15	Nalmefene	50	1.9 $\pm$ 0.5	1.3-2.8
6	Naltrexone	100	2.0$\pm$0.8	1.1-3.4
10	Naltrexone	50	2.4 $\pm$ 0.6	1.4 -3.1

be comparable to that of 3 mg carfentanil and avoids the problems associated with large volumes.

A mean immobilization time of 3.6 minutes (n = 59) is consistently rapid. Immobilization time is dependent on many factors including absorption rate and lipid solubility, but the most important are dart placement and dosage of the immobilizing agent (Haigh 1977, Haigh 1990). The pilot of the chase helicopter and the dart-gunner were both very experienced and this contributed to consistently good dart placement. The use of the long-acting antagonists Nalmefene HCl and Naltrexone HCl and the short duration of action of A-3080 allow the administration of high-dose A-3080 which induces immobilization rapidly and thus minimizes the stress of induction. The 10 mg dose was large enough for rapid immobilization of adult bulls and was safe for calves, as all moose were sternally recumbent and tractable upon arrival at the horse trailer. The smaller moose tolerated the A-3080 well, the mean temperature of the 12 calves was 39.9 $\pm$ 1.7 C which is not considered hyperthermic (Roussel 1975, Schmitt 1988).

A-3080 and Nalmefene HCl or Naltrexone HCl are safe immobilizing drug combinations that resulted in no narcotic recycling or capture myopathy. Lack of recycling is due to both the short duration of action of A-3080 (half-life still unknown) and the comparatively long duration of action of Nalmefene HCl and Naltrexone HCl. Naltrexone HCl has an elimination half-life of 3.9 hours in humans with an active major metabolite, 6-B-naltrexol, that has an elimination half-life of 12.9 hours (Haigh 1990, Stanley *et al.* 1988, Verebey 1976). Nalmefene HCl is about 12 times more potent then Naltrexone HCl in the rat but has an elimination half life of only about 2 hours (Dixon 1986, Jacobson 1988).

No capture myopathy was observed, even though the total length of time the animal was manipulated (from the time of initial pursuit to release at the relocation site) was several hours (this data was not recorded). This is probably due to an abbreviated pursuit and rapid immobilization times. The combination of a large dose of a potent, rapidly acting yet short duration immobilizing agent and a long duration antagonist may have also minimized the chances for capture myopathy to occur. We believe that future advances in chemical immobilization will most likely come via the development of still more potent, rapid acting yet extremely short lasting immobilizing agents and even longer duration antagonists. Drugs which have high safety margins or therapeutic indices allow larger doses to be used which usually shortens the time to drug onset. Rapid onset when combined with a drug with a short Tmax (time to maximal blood concentration) ensures rapid onset of immobilization. If the immobilizing agent also has a rapid redistribution and short elimination half time, recovery is short. If reversal of the rapid acting, short duration immobilizing agent is accomplished with a long lasting antagonist, it would appear that the chances of capture myopathy due to slow onset of immobilization or re-narcotization after reversal should be minimized. The Tmax and redistribution and elimination times of A-3080 have yet to be determined but clinically they appear to be shorter than those of carfentanil. Whether these apparent features of A-3080 and the long durations of action of naltrexone and nalmefene will reduce the incidence of capture myopathy in moose and other ungulates will have to be determined in carefully performed comparisons of these drugs to those that are currently available.

ACKNOWLEDGEMENTS

We are indebted to the Utah Division of Wildlife Resources, Ogden, Utah, and Anesta Corp., Salt Lake City, Utah, for their assistance and cooperation in this research. This study was partially supported by the Stanley Research Foundation. We would like to thank

Warren Rogers for his skill and dedication.

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