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EVALUATION OF XYLAZINE HYDROCHLORIDE AS THE SOLE IMMOBILIZING AGENT IN MOOSE AND CARIBOU— AND ITS SUBSEQUENT REVERSAL WITH IDAZOXAN

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ABSTRACT: Xylazine hydrochloride was used as the sole immobilizing agent in moose and caribou. The animals were free-ranging and immobilization was accomplished from a helicopter using powered darts. Following a period of immobilization during which radiotelemetry collars were fitted, the animals were revived using idazoxan (RX 781094) or its methoxy analogue RX 821002. Xylazine was administered at dose rates of approximately 3.0 mg/kg and 5.0 mg/kg to the moose and caribou, respectively. Moose received 430 ± 27 mg of xylazine and a mean dose of 10 mg idazoxan (RX 781094). Caribou received 485 ± 30 mg xylazine and a mean dose of 4 mg idazoxan (RX 821002). This technique gave adequate immobilization with rapid recovery of consciousness in both species.

Key words: Moose, *Alces alces*, caribou, *Rangifer tarandus*, chemical immobilization, xylazine hydrochloride, reversal, idazoxan.

INTRODUCTION

Xylazine hydrochloride is commonly used in the capture of wild animals, either alone, or in combination with agents such as ketamine hydrochloride. It is an alpha$_2$ adrenergic agonist with sedative, hypnotic and analgesic properties (Hsu, 1981). It exerts its sedative properties via alpha$_2$ adrenoceptors in the locus coeruleus (Van Zwieten et al., 1983). Reversal of xylazine-induced sedation has been frequently attempted using specific alpha$_2$ antagonists such as yohimbine (Hsu, 1983) and tolazoline (Tranquilli et al., 1984) and non-specific agents such as 4-aminopyridine and doxapram (MacKintosh and Van Reenen, 1984).

The completeness of xylazine reversal when using yohimbine appears to be species related. In moose (*Alces alces*) and caribou (*Rangifer tarandus*) as well as in domestic cattle and sheep, yohimbine produces only partial reversal. In domestic dogs and cats more complete reversal may be expected (author's observations).

Idazoxan (RX 781094), (2-(2-(1,4-benzodioxanyl)-2)imidazoline-hydrochloride), is an alpha$_2$ antagonist with little alpha$_1$ activity (Doxey et al., 1983). The respective ED_{50} of idazoxan and yohimbine at alpha$_2$ cells of the locus coeruleus are 17 and 592 μg/kg (Marwaha and Aghajanian, 1982). In holstein calves, idazoxan at either 0.05, 0.075 or 0.10 mg/kg intravenously (i.v.) produced rapid and complete reversal of xylazine-induced sedation (Doherty et al., 1987). No serious adverse affects have been attributed to idazoxan administration in either calves or humans (Elliott et al., 1984; Doherty et al., 1987).

Substance RX 821002 is a 2-methoxy analogue of idazoxan. Its alpha$_2$ antagonist properties are greater than those of idazoxan, both in vivo and in vitro (Technical Publication, Reckitt and Colman, Pharmaceutical Division, Hull, England). RX 821002 is more selective in its alpha$_2$ antagonism and appears to be devoid of alpha$_1$ agonist activity. In addition, RX 821002 is 10 times more potent than idazoxan in preventing clonidine induced EEG changes in the rabbit (Technical Publication, Reckitt and Colman).

The purpose of the study was to determine the effectiveness of xylazine as an immobilizing agent when used alone and to evaluate idazoxan and its analogue RX 821002 as reversal agents.

MATERIALS AND METHODS

The study was conducted on free-ranging moose (*Alces alces americana*, n = 20) and woodland caribou (*Rangifer tarandus*, n = 132)

in Newfoundland (48° to 49°N, 54° to 57°W). All animals were darted with xylazine hydrochloride (Rompum, Haver-Lockhart, Bayvet Division, Etobicoke, Ontario, Canada M9W 1G6) using Cap-Chur equipment (Palmer Chemical and Equipment Company, Douglasville, Georgia 30134, USA) fired from a helicopter. The purpose of the immobilization was the collection of biological data to determine the effects of development, namely logging, mining and hydro-electric projects on wildlife populations in central and southwestern Newfoundland. Radiotelemetry collars were fitted to all animals and their progress was monitored in the 2 hr following release and at irregular intervals over the succeeding months. Xylazine hydrochloride (100 and 300 mg/ml) was administered intramuscularly (i.m.) at approximately 3.0 mg/kg to the moose with 5 to 8 mg/kg being given to the caribou. The 300 mg/ml solution was prepared by dissolving 3.0 g of the dried substance in 10 ml of sterile water. As the caribou ranged in weight (57 to 155 kg) the xylazine dose varied (450 to 750 mg). A large male caribou with an estimated body weight of 350 kg was immobilized with 750 mg of xylazine in 5 min and 50 sec. The moose were estimated to weigh 115 to 160 kg and the xylazine dose varied accordingly (350 to 500 mg).

The moose were darted on primarily wooded terrain. In order to reduce the risks of capture myopathy, pursuit was restricted to 2 min, after which time if the animal had not been successfully darted the attempt was abandoned. In contrast, caribou were darted on open bogland or dry barrens. Following a mean immobilization time of 32 min (2 to 41 min), idazoxan (RX 781094, Reckitt and Colman, Kingstone upon Hull, England) or its methoxy analogue (RX 821002) was administered to the moose and caribou respectively. Both drugs were given i.v. at approximate dose rates of 0.06 mg/kg. The mean dose of RX 781094 administered to the moose was 10 mg and the caribou received RX 821002 at a mean dose of 4 mg.

The time taken to induce recumbency was recorded together with the time to standing following antagonist injection. The mean and the standard error of the mean ($\bar{x} \pm$ SEM) were calculated for each parameter.

RESULTS

Intramuscular xylazine hydrochloride at the above dose rates was successful in inducing sedation and recumbency on all occasions. However, when using the 100 mg/ml solution inconsistent results were found and three caribou had to be darted twice. This problem was solved with the use of the more concentrated solution (300 mg/ml). We believe that some of the drug solution was lost on impact through the injection tract when using larger injectate volumes. The mean time to recumbency was 6 min and 22 sec (Table 1). Of the three caribou which were darted twice one had an induction time of 41 min. Two animals were slow to respond to the reversal agent and one had a recovery time of over 8 min (Table 1). These animals may have received part of the reversal solution perivascularly because they appeared to respond in a similar fashion to animals which had received lower doses of reversal in an earlier trial (T. J. Doherty and D. P. R. Tweedie, unpubl. data).

One caribou died apparently from the direct effects of darting due to pneumothorax and intrathoracic hemorrhage. Another caribou died from respiratory failure before reversal could be attempted; it had been recumbent for 26 min following a 4 min induction time. Reversal was consistently preceded by a brief period of apnea followed by a period of deep breathing with some ear twitching. Animals then assumed sternal recumbency, jumped to their feet and fled. This was often completed in <1 min.

One animal demonstrated a brief period of excitement following RX 821002. It ran away, jumping wildly and shaking its head. Idazoxan and RX 821002 produced complete reversal of sedation and most animals were alert and mobile within 2 min (Table 1).

DISCUSSION

When considering the properties of an ideal immobilizing drug for use in wild animals the following factors are important. The drug should possess good bioavailability following i.m. injection, producing a rapid onset of sedation. As the volume of injectate in a single dart is limited, the drug should be potent in small volumes. The duration of action must be suited to the procedure in question and

TABLE 1. Time to induction postxylazine and time to recovery postidazoxan (RX 781094 and RX 821002) in moose and caribou, respectively. Induction time indicates time taken to induce recumbency. Recovery time indicates time to standing. Values are expressed in minutes.

Species	n	Variable	$\bar{x}$	SE	Maximum value	Minimum value
Caribou	132	Induction time (min)	6.3	0.65	41.0	1.0
(*Rangifer tarandus*)		Recovery time (min) (RX 821002)	1.6	0.15	8.5	0.5
Moose	20	Induction time (min)	5.1	0.45	9.0	2.75
(*Alces alces*)		Recovery time (min) (RX 781094)	1.6	0.15	3.3	0.66

ideally the drug effects should be reversible. Operator safety is a primary consideration and this factor becomes very important when darting animals from the cramped quarters of a helicopter. The use of potent opioids carries a high risk to personnel and makes retrieval of off-target darts desirable. Drug cost is another factor in addition to commercial availability.

The combination of xylazine and idazoxan fulfills most of the above requirements, however, disadvantages do exist. Xylazine hydrochloride is associated with bradycardia and cardiovascular depression in ruminants (Campbell et al., 1975). In this study the lowest heart rate recorded in the moose was 34 beats per min with a mean rate of 45. Heart rates were not recorded in the caribou. When xylazine is used as the sole immobilizing agent very large doses are required to achieve consistent and relatively fast anesthesia. Consequently, recumbency is prolonged which increases the likelihood of bloat and regurgitation. Myopathy may result from recumbency and struggling. Hyperthermia develops postxylazine and thermoregulation may be impaired for up to 12 hr (Young, 1979). The need for an effective antagonist becomes greater under these circumstances because partial reversal will leave the animals susceptible to predation and physical injury.

Opioids such as fentanyl, carfentanyl and etorphine are still widely used to immobilize wild animals (Plotka et al., 1987). They possess extreme potency and consequently pose a problem from the human safety aspect. Other disadvantages include high cost, dose dependent respiratory depression in all species and the requirement to keep accurate drug records. Advantages of the newer opioids include a higher therapeutic index and fewer side effects than older and less potent drugs such as meperidine (Niemegeers et al., 1976). Specific antagonists are available, however, resedation several hours postreversal is not uncommon due to enterohepatic opioid circulation (Hall and Clarke, 1983).

Idazoxan and its 2-methoxy analogue proved to be excellent reversal agents for xylazine. Animals were immediately capable of negotiating streams, ponds and fallen trees over the rough terrain. Most female caribou had young calves and some had calved within the previous 12 hr. Many were observed accurately scenting their calves over considerable distances immediately postreversal, indicating no apparent reduction in maternal bonding or olfactory function. A mean RX 821002 dose rate of 0.06 mg/kg gave best results in the caribou. Considering the relative potency of RX 781094 and RX 821002 it is surprising that similar dose rates were needed. However, this is possibly explained by the higher dose rate of xylazine needed in the caribou. Overdosing with idazoxan is manifested by transient excitement and death may result if overdosing is excessive. However, this is unlikely, considering that the acute toxicity (LD_{50}) of RX 821002 in mice is 13.9 mg/kg (Technical Publication, Reckitt and Colman).

In conclusion, our study indicated that xylazine-idazoxan is an effective combination for immobilization and revival of these two species of wild ruminants. Consistent results were achieved when using xylazine at a concentration of 300 mg/ml. Idazoxan (RX 781094) and its methoxy analogue RX 821002 rapidly reversed the effects of xylazine and resedation was not observed.

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