YOHIMBINE HYDROCHLORIDE AS AN ANTAGONIST TO XYLAZINE HYDROCHLORIDE–KETAMINE HYDROCHLORIDE IMMOBILIZATION OF WHITE-TAILED DEER

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Source: Journal of Wildlife Diseases, 21(4) : 405-410

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-21.4.405

Journal of Wildlife Diseases, 21(4), 1985, pp. 405–410

YOHIMBINE HYDROCHLORIDE AS AN ANTAGONIST TO XYLAZINE HYDROCHLORIDE–KETAMINE HYDROCHLORIDE IMMOBILIZATION OF WHITE-TAILED DEER

L. David Mech,[1,2] Glenn D. Del Giudice,[3] Patrick D. Karns,[4] and Ulysses S. Seal[5]

ABSTRACT: Thirteen captive and one free-ranging white-tailed deer (*Odocoileus virginianus*) were immobilized one to six times each with ketamine hydrochloride and xylazine hydrochloride during winter and spring in northern Minnesota. Administration of 0.09 to 0.53 mg of yohimbine hydrochloride per kg IV after each trial reversed the immobilization. The deer raised their heads within a median time of 2.0 min, stood in 6.0 min and walked away in 9.5 min. No adverse side effects were observed for several weeks following the immobilization.

INTRODUCTION

Pharmacological immobilization of white-tailed deer is often difficult because of side-effects (e.g., excitement, respiratory depression, diaphragm paralysis, body-temperature changes, bloat, regurgitation) that often accompany the use of drugs (Bauditz, 1972; Dean et al., 1973; Roughton, 1975).

Xylazine hydrochloride has been used for immobilizing captive and free-ranging deer (Bauditz, 1972; Roughton, 1975; Mautz et al., 1980; Jacobsen, 1983; Jessup et al., 1983; Warren et al., 1984), and combinations of xylazine hydrochloride and ketamine hydrochloride have been used to immobilize mule deer (*O. hemionus*) (Jessup et al., 1983), Rocky Mountain elk (*Cervus elaphus*), bison (*Bison bison*), pronghorn (*Antilocapra americana*) (Wentges, 1975), and feral pigs (*Sus scrofa*) (Baber and Coblentz, 1982). However these drugs may result in down times of 12 hr or more (Seal, unpubl. data; Karns, unpubl. data; Mech, unpubl. data), depressed body temperatures, and the various physiological and environmental hazards associated with such conditions (Jessup et al., 1980). In mule deer these problems were overcome by the use of yohimbine hydrochloride as an antagonist (Jessup et al., 1983). Hsu and Shulaw (1984) demonstrated the effectiveness of yohimbine hydrochloride as an antagonist to xylazine hydrochloride in immobilized white-tailed deer during single trial tests, at a dose of 0.1 mg/kg (Hsu and Skulaw, 1985).

We tested yohimbine hydrochloride in white-tailed deer that were immobilized with a xylazine hydrochloride–ketamine hydrochloride combination during multiple trials, and herein report the results.

Received for publication 28 September 1984.

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MATERIALS AND METHODS

Our tests were conducted during February through early May 1984 in northern Minnesota under two sets of conditions: (1) with captive deer immobilized by xylazine hydrochloride (Rompun, Haver-Lockhart, Bayvet Division, Miles Laboratory, Inc., Shawnee, Kansas 66201, USA) and ketamine hydrochloride (Ketaset, Bristol Veterinary Products, Division of Bristol Myers, Syracuse, New York 13201, USA), and (2) with a wild deer also immobilized by a xylazine hydrochloride–ketamine hydrochloride combination. The captive deer were maintained in separate outdoor enclosures near

TABLE 1. Penned white-tailed deer immobilized by a xylazine hydrochloride–ketamine hydrochloride combination, which was then reversed by intravenous yohimbine hydrochloride.

Deer no.	Age[a]	Sex[b]	Body weight range (kg)	No. times tested	Immobilizing drugs: Xylazine hydrochloride dosage (mg/kg) Mean (SE)	Immobilizing drugs: Ketamine hydrochloride dosage (mg/kg) Mean (SE)	Induction time (min) Mean (SE)	Yohimbine hydrochloride dosage (mg/kg) Mean (SE)	Time to head up (min) Mean (SE)	Time to standing (min) Mean (SE)	Time to walking (min) Mean (SE)
6206	A	F	57.0–65.5	6	1.26 (0.02)	6.48 (0.89)	15.3 (2.7)	0.29 (0.03)	4.3 (2.9)	4.7 (3.5)	8.7 (6.7)
5264	A	F	58.2–59.5	4	1.28 (0.01)	7.64 (1.25)	13.5 (1.2)	0.25 (0.06)	23.5 (11.2)	25.8 (10.2)	26.5 (11.5)
6155	Y	F	52.7–54.1	4	1.40 (0.01)	5.96 (0.09)	7.3 (3.6)	0.30 (0.03)	6.7 (4.7)	9.0 (3.8)	9.0 (4.4)
5267	A	F	45.9–50.5	5	1.59 (0.03)	7.79 (1.19)	6.6 (2.7)	0.34 (0.02)	6.4 (1.6)	10.0 (4.7)	12.0 (05.7)
6247	A	F	46.8–50.0	3	1.38 (0.19)	6.19 (0.60)	3.7 (0.9)	0.34 (0.03)	1.3 (0.3)	4.3 (2.9)	5.0 (2.6)
6162	Y	F	41.8–45.9	5	1.69 (0.03)	6.92 (0.52)	6.4 (1.6)	0.36 (0.04)	3.2 (1.2)	5.4 (2.4)	5.0 (3.0)
6241[c]	A	F	45.5–50.5	4	1.53 (0.04)	7.39 (1.45)	8.3 (4.0)	0.36 (0.04)	2.0 (1.4)	6.8 (4.9)	18.0 (8.6)
6204[c]	A	F	49.1–50.0	2	1.52 (0.02)	9.64 (5.15)	19.5 (15.5)	0.28 (0.04)	7.0 (5.0)	42.0	—
6168[c]	A	F	40.5–52.7	5	1.53 (0.13)	8.48 (1.37)	10.0 (3.8)	0.34 (0.04)	11.2 (5.3)	22.8 (8.0)	23.0 (13.7)
6222	A	M	84.5–91.8	2	0.72 (0.18)	4.92 (1.07)	12.0 (5.0)	0.26 (0.02)	1.5 (0.5)	1.5 (0.5)	1.5 (0.5)
6185	—	F	37.7	1	1.99	5.97	10.0	0.53	22.0	23.0	—
6220	—	M	72.7	1	0.69	11.69	23.0	0.28	5.0	19.0	19
6620	—	M	80.9	1	0.93	06.94	22.0	0.31	14.0	14.0	36

[a] A = adult, Y = yearling.
[b] F = female, M = male.
[c] Deer fasted for first 24 days of study including two tests with yohimbine.

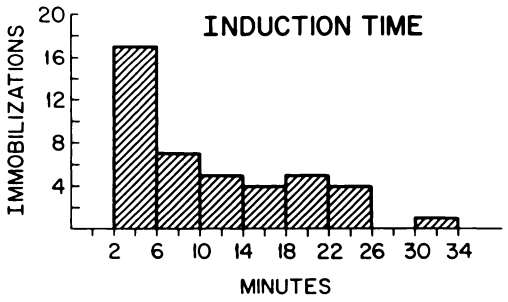

FIGURE 1. Frequency distribution of induction time for white-tailed deer immobilized with a xylazine hydrochloride–ketamine hydrochloride combination.

Grand Rapids, Minnesota and fed commercial deer pellets (Ozoga, 1978), although three of them were fasted for the first 24 days as part of an ongoing nutritional study. Thirteen individuals, males and females, were tested for a total of 43 immobilizations (Table 1).

Each captive deer was injected intramuscularly (IM) via jabstick with 50–75 mg of xylazine hydrochloride (0.54 to 1.99 mg/kg) and 325 mg of ketamine hydrochloride (3.78 to 14.77 mg/kg) (Table 1). Supplemental IM injections of up to 600 kg of ketamine hydrochloride were often necessary for effective immobilization. After periods ranging from 17 to 259 min, during which the deer were weighed, blood-sampled, catheterized for urine, and otherwise examined, each individual was injected intravenously (IV) with 5 to 30 mg of yohimbine hydrochloride (Sigma Chemical Co., P.O. Box 14508, St. Louis, Missouri 63178, USA) (1 mg/ml of sterile saline, 0.09 to 0.52 mg yohimbine hydrochloride/kg). One animal was too active to be injected IV; therefore 10 mg of yohimbine hydrochloride was given IM. The deer were then observed for up to 49 min and checked periodically afterwards for 2 wk.

Tests with wild deer involved a 72- to 76-kg doe captured three times by rocket net and injected IM by hand with 0.9 mg xylazine hydrochloride and 8.0 to 8.3 mg ketamine hydrochloride/kg. This animal was maintained under anesthesia for 34 to 137 min via supplemental IM injection of 4.2 to 11.8 mg of ketamine hydrochloride/kg as blood samples were taken and the animal was weighed and otherwise processed. Some 18 to 34 min after last injection, she was administered 0.20 to 0.28 mg of yohimbine hydrochloride/kg IV, and her behavior observed for up to 99 min after yohimbine administration.

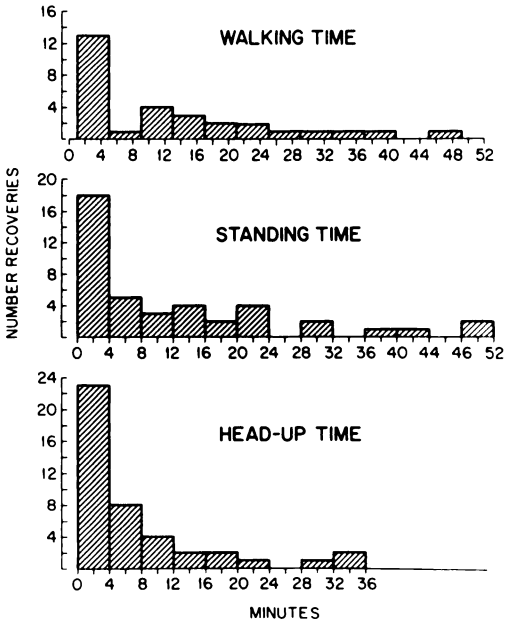

FIGURE 2. Frequency distributions of yohimbine hydrochloride-response times by white-tailed deer immobilized with a xylazine hydrochloride–ketamine hydrochloride combination.

RESULTS

Induction time (i.e., the interval between the initial injection and the deer's inability to stand) for captive deer drugged with xylazine hydrochloride and ketamine hydrochloride ranged from 2 to 35 min (med. = 8.0, SE = 1.2) (Fig. 1, Table 1). Supplemental administration of 0 to 21 mg of ketamine hydrochloride per kg IM usually maintained anesthesia for 17 to 191 min.

Intravenous administration of 0.09 to 0.53 mg of yohimbine hydrochloride per kg to the captive deer was generally followed by rapid recovery (Table 1). Often within seconds and usually within a few min (med. = 2.0, SE = 1.6), the animal would lift its head first, begin moving its legs, stand (med. = 6.0 min, SE = 2.1), and walk away (med. = 9.5 min, SE = 2.9) (Fig. 2). For at least 3 hr after arising, the animals either continued to walk around normally in the pen, or lay in the shade

with their heads up. They were responsive to stimulation and appeared to behave normally. No adverse reactions or effects were seen in these deer the next day or for any period up to 14 days after initial treatment, even though most of these animals were immobilized in this fashion four to six times at 14-day intervals. The mean times to standing and walking in fasted deer (29.2 ± 7.8 and 33.7 ± 7.3 min) were greater ($P < 0.025$) than in nonfasted deer (9.4 ± 1.8 and 10.2 ± 2.1 min).

A 59-kg doe inadvertently given 775 mg of xylazine hydrochloride recovered normally after administration of 2 liters of lactated Ringer's solution subcutaneously, 12 mg (0.20 mg/kg) of yohimbine hydrochloride IM, and 28 mg (0.47 mg/kg) of yohimbine hydrochloride IV 3–4.5 hr after xylazine hydrochloride administration. She was drugged again with the usual xylazine hydrochloride–ketamine hydrochloride combination five times during the next 10 wk.

The wild deer recovered similarly to the captive deer during a period when temperatures reached −12 C.

DISCUSSION AND CONCLUSIONS

Jessup et al. (1983) reversed the effects of xylazine hydrochloride–ketamine hydrochloride in mule deer using 0.125 mg/kg of yohimbine hydrochloride IV. A dose of 0.1 mg/kg of yohimbine hydrochloride also reversed the effects of xylazine hydrochloride-induced immobilizations of white-tailed deer (Hsu and Shulaw, 1985). We found yohimbine hydrochloride to be a practical and effective antagonist for xylazine hydrochloride–ketamine hydrochloride immobilization of white-tailed deer (Fig. 2). Although we used yohimbine hydrochloride doses two to three times those used by Jessup et al. (1983) on mule deer, our deer became mobile after a similar period post-injection. Absence of a decreased response time to the larger doses of yohimbine hydrochloride suggests that a threshold dose of about 0.26 mg/kg exists for deer, and we recommend this dose. Hsu and Shulaw (1984) reported that white-tailed deer injected with yohimbine hydrochloride after being immobilized with xylazine hydrochloride alone could stand after a shorter period ($\bar{x} = 4.4$ min) than could our deer. Possibly this was because our deer received xylazine hydrochloride and ketamine hydrochloride.

Three extreme situations during the present study lend additional support to the claim that yohimbine hydrochloride is not only safe in itself for the periods involved in this study but also effective in countering adverse conditions that otherwise might have rendered xylazine hydrochloride–ketamine hydrochloride immobilization of deer fatal. First is the accidental injection of an adult doe with 13 mg xylazine hydrochloride per kg, a dose seven times that required for immobilization. Ordinarily, without constant attention for perhaps days, this animal would have been expected to die (Seal, unpubl. data; Karns, unpubl. data). However, relatively moderate amounts of yohimbine hydrochloride countered this effect. In fact, the experience with this doe further suggests that a threshold dose exists for yohimbine hydrochloride effectiveness, for only 40 mg of yohimbine hydrochloride (0.68 mg/kg), administered over an 80-min period, was able to reverse the effects of 775 mg of xylazine hydrochloride. Hatch et al. (1982) reversed a 5× xylazine hydrochloride overdosage (11.0 mg/kg) in six dogs using a combination of yohimbine hydrochloride (0.125 mg/kg) and 4-aminopyridine (0.3 mg/kg).

Second, three of our captive does were immobilized and brought to recovery despite their having been fasted for up to 24 days during which they lost up to 38% of their weight. One of these does even perished of malnutrition some 6 days after

she was last drugged and had recovered. (A necropsy performed by the University of MinnesotaVeterinary Diagnostic Laboratory indicated that the cause of death was malnutrition. No internal or subcutaneous fat remained in any store, and femur marrow fat percentage was 55.)

Third, although rectal temperatures of 40–44 C were measured 18 times in the captive deer, sedation was reversed with yohimbine hydrochloride with no visible complications. Roughton (1975) implicated hyperthermia in the deaths of three captive white-tailed deer immobilized with xylazine hydrochloride after measuring rectal temperatures of 40–44 C. Seal et al. (1978) found in northeastern Minnesota that immobilized deer with rectal temperatures 40.0 C or higher were at a greater risk of dying at or shortly after capture.

Yohimbine hydrochloride is known to reverse xylazine hydrochloride (Hatch et al., 1982; Cronin et al., 1983; Goldberg and Robertson, 1983; Jessup et al., 1983), and ketamine hydrochloride (Hatch and Ruch, 1974; Hatch et al., 1983) by acting as an alpha$_2$-adrenoreceptor blocking agent. Our study demonstrates that it reverses xylazine hydrochloride–ketamine hydrochloride immobilizations of white-tailed deer and is highly useful in preventing the usual side effects of prolonged immobilization in captive and wild deer.

ACKNOWLEDGMENTS

This study was supported by the Big Game Club, the U.S. Fish and Wildlife Service, the Minnesota Department of Natural Resources, and the Veterans Administration Medical Center. We thank the following for assistance: Ken Kerr and Geralyn Phifer, William Paul, Steve Fritts, Mike Nelson, Ed Stege, Kirk Johnson, Jim Lazar, and Roger Welters.

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