Journal of Wildlife Diseases, 24(2), 1988, pp. 322–326

KETAMINE-XYLAZINE ANESTHESIA IN RED-TAILED HAWKS WITH ANTAGONISM BY YOHIMBINE

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ABSTRACT: Five red-tailed hawks (*Buteo jamaicensis*) were anesthetized at weekly intervals with intravenous ketamine hydrochloride (KET, 4.4 mg/kg) and xylazine hydrochloride (XYL, 2.2 mg/kg). Twenty min after anesthesia, yohimbine hydrochloride (YOH, 0.05, 0.10, 0.20 and 0.40 mg/kg) or a control was administered. All doses of YOH significantly reduced the head-up times ($F = 20.84$, $df = 1,24$, $P < 0.0001$) and the standing times ($F = 12.30$, $df = 1,24$, $P < 0.0001$), compared to the control group. The heart and respiratory rates following YOH (all doses) were significantly greater ($P < 0.01$) than the anesthetized rates, but were comparable to the rates observed in restrained, unanesthetized hawks. Yohimbine did not appear to have any significant effect on body temperature. Based upon administration of 4.4 mg/kg KET and 2.2 mg/kg XYL, a dose of 0.10 mg/kg YOH was recommended to achieve antagonism without causing profound cardiovascular or respiratory changes.

Key words: Red-tailed hawk, *Buteo jamaicensis*, ketamine hydrochloride, xylazine hydrochloride, yohimbine hydrochloride, heart rate, respiratory rate, anesthesia, antagonism, experimental study.

INTRODUCTION

The combination of the alpha-2 adrenergic agonist xylazine hydrochloride (XYL) and the cyclohexane, ketamine hydrochloride (KET) has been an effective anesthetic agent in many mammalian (Jessup et al., 1983; Hsu and Lu, 1984; Kreeger et al., 1987) and avian species (Amand, 1980; Haigh, 1981; Samour et al., 1984; Harrison et al., 1985). The synergistic action of XYL with KET results in smooth induction and recovery, improved muscle relaxation, enhanced analgesia, and a decreased total dose of either drug compared to their use alone (Amend, 1972). Typically, the recovery period from this drug combination may be prolonged, but the alpha-2 adrenergic antagonist, yohimbine hydrochloride (YOH) has been shown to effectively reduce the recovery times in many wild and domestic mammalian species (Jessup et al., 1983; Hsu and Lu, 1984; Mech et al., 1985; Kreeger and Seal, 1986b; Kreeger et al., 1987). The use of YOH as a XYL or KET/XYL antagonist in avian species has been demonstrated in 1–3-day-old Leghorn chicks and adult Guineafowl (*Numida meleagris*) (Hsu, 1981; Teare, 1987).

In certain field and clinical studies requiring short-term anesthesia, it would be desirable to antagonize KET/XYL anesthesia. The purpose of this study was to determine the efficacy of YOH antagonism of KET/XYL anesthesia in red-tailed hawks (*Buteo jamaicensis*) and the effects upon their cardiovascular and respiratory parameters.

MATERIALS AND METHODS

Five permanently crippled red-tailed hawks obtained from the Raptor Research and Rehabilitation Program (RRRP; University of Minnesota, St. Paul, Minnesota 55108, USA) were used in the study. There were three males and two females, as determined by endoscopy (weight range 990–1450 g). All birds were two-winged and remained healthy during the study, as determined by physical examinations and hematological parameters. These birds were housed in a large indoor flight room where lighting and temperature were artificially controlled. They were fed killed laboratory rodents or poultry every other day and provided water ad libitum.

The birds were anesthetized at weekly intervals in a crossover design using 4.4 mg/kg ketamine (Ketaset, Bristol Laboratories, Syracuse, New York 13201, USA) and 2.2 mg/kg xylazine

(Rompun, Haver-Lockhart Laboratories, Shawnee, Kansas 66201, USA). These drugs were combined and administered intravenously (i.v.) in the basilic vein. Since induction generally occurred in <10 sec, the time of injection was considered the start of the 20 min anesthesia period. The feet were taped for operator safety and the birds were placed in dorsal recumbancy on a padded table.

Yohimbine hydrochloride (Sigma Chemical Company, St. Louis, Missouri 63178, USA) was dissolved in sterile saline to yield a solution containing 0.5 mg/ml YOH. At 20 min postinduction, the hawks were given one of four doses of YOH (0.05, 0.10, 0.20 and 0.40 mg/kg) i.v., or an equivalent volume of sterile 0.9% saline.

Heart rates (HR) and respiratory rates (RR) were monitored during the preanesthesia period, the 20-min anesthesia period (5-min intervals) and the 10-min recovery period (1-min intervals following YOH). The RR were counted by visual inspection and HR were measured using an electrocardiograph (Datascope 871 Monitor, Datascope Corp., Paramus, New Jersey 07652, USA). Body temperatures were monitored during the anesthesia and recovery periods using a cloacal probe (Monitemp Digital Temperature Recorder, American Hospital Supply, Minneapolis, Minnesota 55402, USA). The temperature probes were usually expelled from the cloaca within 5 min following YOH due to increased muscle tone and activity.

Head-up times (HUT) and standing times (ST) were recorded following YOH. The HUT was the time at which the hawk opened its eyes and raised its head. The ST was the time required for the bird to stand unassisted by wing or tail support without ataxia.

Statistical analysis were by two-way analysis of variance and Tukey's Pairwise Comparisons. A P-value of ≤ 0.05 was considered significant (Snedecor and Cochran, 1980).

RESULTS

The HUT and ST after YOH administration were significantly shorter ($P < 0.0001$) than those of the control group (Table 1). These effects were observed at the lowest doses of YOH and no significant improvements were gained using the higher YOH doses. Statistically, there were no differences between the four YOH groups for these parameters.

During anesthesia, the HR were significantly lower ($P < 0.0001$) than prior to anesthesia (Fig. 1). Administration of the control solution did not alter the HR in the anesthetized birds ($P > 0.05$; Fig. 2). Following YOH administration (all doses), the HR were higher ($P < 0.01$) than those recorded during the anesthesia period. During the first 3 min following YOH, there was a steep linear increase in HR for the three higher doses ($r = 0.8211$, $P < 0.0001$, $n = 45$), after which the rates tended to stabilize. The time interval between 2 and 5 min postYOH was used to compare the effects of different doses on HR and RR (Table 2). This interval represents the maximal response to YOH. Because of the birds arousal following YOH, observations beyond 5 min had enough missing data points to prevent precise statistical analysis. The HR following 0.10 and 0.20 mg/kg YOH were not significantly different from each other during this interval, but were higher than the control and 0.05 mg/kg groups and lower than the 0.40 mg/kg group ($P < 0.05$; Table 2).

The RR were lower during anesthesia ($P < 0.01$) than prior to anesthesia (Fig. 1). Administration of the control (saline) did not alter the RR in the anesthetized hawks ($P > 0.05$). Following YOH administration, there was a significant increase ($P < 0.05$) in RR compared to those observed during anesthesia (all doses). The mean RR observed during the interval from

TABLE 1. Head-up (HUT) and standing times (ST) for red-tailed hawks anesthetized with 4.4 mg/kg ketamine and 2.2 mg/kg xylazine, followed by yohimbine (YOH) administration.

Dose of YOH (mg/kg)	n	HUT (min) Mean ± SE Range	ST (min) Mean ± SE Range
Control	5	14.6 ± 2.6 10–24	86.4 ± 16.0 47–124
0.05	5	4.2 ± 1.5[a,b] 1–9	31.6 ± 9.2[a,b] 9–63
0.10	5	1.2 ± 0.2[a,b] 1–2	12.8 ± 4.4[a,b] 5–30
0.20	5	1.2 ± 0.2[a,b] 1–2	15.6 ± 2.4[a,b] 9–24
0.40	5	1.0[a,b] 1	14.4 ± 2.8[a,b] 7–22

[a] Significantly different from control value at $P < 0.05$.
[b] No significant difference between YOH doses at $P > 0.05$.

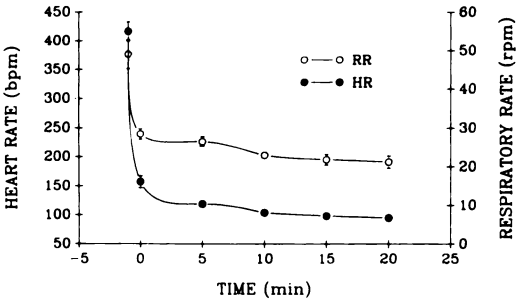

FIGURE 1. Heart rates (beats per min; bpm) and respiratory rates (respirations per min; rpm) in red-tailed hawks immediately prior to anesthesia (restrained), and for 20 min following i.v. administration of 4.4 mg/kg ketamine and 2.2 mg/kg xylazine. Symbols without error bars had very small standard errors.

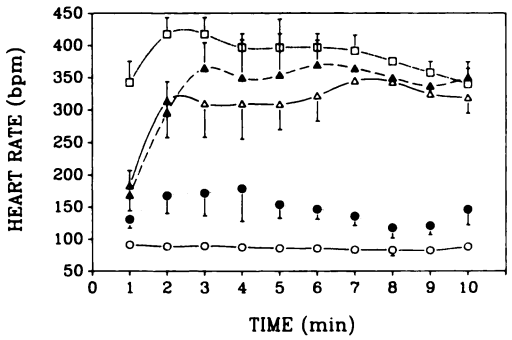

FIGURE 2. Heart rates (beats per min; bpm) following i.v. administration of a control (○); 0.05 mg/kg yohimbine (YOH) (●); 0.10 mg/kg YOH (△); 0.20 mg/kg YOH (▲); 0.40 mg/kg YOH (□). Symbols without error bars had very small standard errors.

2 to 5 min were not statistically different from each other following 0.05 and 0.10 mg/kg YOH ($P > 0.05$), but were higher than the control group and lower than the 0.20 and 0.40 mg/kg YOH groups ($P < 0.05$; Table 2).

The HR and RR following all doses of YOH were not as high as those observed in restrained hawks prior to anesthesia (Table 2).

Body temperatures decreased from 40.5 ± 0.2 C to 40.0 ± 0.2 C during anesthesia (20 min). No significant changes in body temperature were noted following YOH administration ($P > 0.05$).

TABLE 2. Heart (HR) and respiratory (RR) for red-tailed hawks anesthetized with 4.4 mg/kg ketamine and 2.2 mg/kg xylozine, followed by yohimbine (YOH) administration (mean ± SE for data collected between 2 and 5 min). Preanesthesia (restrained) HR and RR are included for comparison.

YOH dose (mg/kg)	HR (bpm)[a]	RR (rpm)[a]
Control	88.2 ± 3.1	20.5 ± 1.5
0.05	167.8 ± 16.5[c]	30.2 ± 1.7[c]
0.10	315.1 ± 23.3[c]	35.7 ± 2.0[c]
0.20	333.4 ± 24.6[c]	42.7 ± 2.7[c]
0.40	408.6 ± 11.3[c]	40.4 ± 1.1[c]
Preanesthesia[b]	416.5 ± 16.7	49.1 ± 3.8

[a] Bpm, beats per min; rpm, respirations per min.
[b] Preanesthesia data represent an average of 1 min prior to induction.
[c] Significantly different from control value at $P < 0.05$.

DISCUSSION

Xylazine is an alpha-2 adrenergic agonist that stimulates central presynaptic adrenoceptors, preventing norepinephrine release at the nerve terminal to produce sedation and analgesia (Starke, 1977; Doxey and Roach, 1980). In many avian species, XYL does not produce immobilization adequate for most surgical procedures. Other problems include respiratory depression, hypotension, bradycardia, excitement and convulsions in both mammals and birds, and prolonged recovery times of up to 12 hr (Amand, 1980; Hatch et al., 1982; Samour et al., 1984).

The site of action of ketamine has yet to be defined, but may include cholinergic, serotonergic, dopaminergic, or opioid receptors (Finck and Ngai, 1982; White et al., 1982; Leeuwin et al., 1984). Ketamine has limited use as an avian anesthetic agent when used alone because of inadequate analgesia and muscle relaxation during surgery and sometimes violent recoveries (Boever and Wright, 1975; Altman, 1980; Redig et al., 1984; Samour et al., 1984). Variability to response by different avian species has been reported (Redig and Duke, 1976).

Yohimbine is an alpha-2 adrenergic antagonist (Goldberg and Robertson, 1983) that has been used extensively to reverse

XYL or KET/XYL anesthesia in many domestic (Hsu, 1983; Hsu and Lu, 1984) and wild mammals (Jessup et al., 1983; Mech et al., 1985; Ramsey et al., 1985; Kreeger and Seal, 1986b; Kreeger et al., 1987), and in two avian species (Hsu, 1981; Teare, 1987).

The effect of YOH reversal of KET anesthesia is more controversial. It has been suggested that YOH acts as a central stimulant to override some of the effects of KET (Hsu and Lu, 1984). However, in certain mammals anesthetized with KET followed by YOH antagonism, there was no reduction in walk time (Hatch et al., 1982; Kreeger and Seal, 1986a). Red-tailed hawks anesthetized with 30 mg/kg i.v. KET, followed by 0.10 mg/kg YOH did not have shorter recovery times when compared to controls (Degernes, unpubl. data).

The KET/XYL anesthetic dose routinely used in red-tailed hawks at the Raptor Research and Rehabilitation Program is 10.0 mg/kg KET and 2.0 mg/kg XYL, combined and administered i.v. (Redig, unpubl. data). In pilot studies, we found that hawks anesthetized with this 5:1 KET/XYL ratio exhibited difficult recoveries following YOH antagonism, presumably due to the cataleptic effects of residual KET after XYL had been antagonized. After experimentation, we determined that 2:1 KET/XYL (4.4 mg/kg KET and 2.2 mg/kg XYL) provided the lowest possible dose of KET to achieve an adequate level of anesthesia for short-term diagnostic or surgical procedures (under 15 min). By using the reduced dose of KET, YOH antagonism of XYL resulted in smoother recoveries for the hawks. Other researchers have found this 2:1 ratio (4.0 mg/kg KET and 2.0 mg/kg XYL) to be effectively antagonized by YOH in coyotes (Kreeger and Seal, 1986b).

The four YOH doses were selected to determine the optimum reversal dose with the fewest side effects. The rise in HR and RR following all doses of YOH were not as high as those observed in restrained, preanesthetized birds, and therefore are probably not pharmacologically induced. Yohimbine has been shown to cause minimal effect on HR as a result of direct cardiac action (Gomes et al., 1980). At no time were any ECG abnormalities recorded for any of these hawks.

CONCLUSIONS

A dose of 4.4 mg/kg KET and 2.2 mg/kg XYL provided adequate short-term anesthesia for red-tailed hawks. A dose of 0.10 mg/kg YOH was the lowest dose required to significantly reduce HUT and ST and did not result in profound cardiovascular or respiratory responses.

ACKNOWLEDGMENTS

We would like to thank Susan B. Chaplin for her editorial assistance. The monitoring equipment was provided by the Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota. This work was supported by the University of Minnesota Raptor Research and Rehabilitation Program.

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Received for publication 26 June 1987.