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Immobilization of Coyotes with Xylazine Hydrochloride–Ketamine Hydrochloride and Antagonism by Yohimbine Hydrochloride

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Many wild carnivores have been immobilized with a combination of the alpha$_2$-adrenergic agonist, xylazine hydrochloride (HCl), and the cyclohexane, ketamine HCl (Hebert and McFetridge, 1981, Chemical Immobilization of North American Game Animals, Alberta Energy and Nat. Res., Alberta, Canada, 250 pp.; Parry et al., 1981, J. Wildl. Manage. 45: 986–990; Nielsen et al., 1982, Chemical Immobilization of North American Wildlife, Wisconsin Humane Society, Milwaukee, Wisconsin, USA, 447 pp.; Fuller and Kuehn, 1983, J. Wildl. Dis. 19: 69–72; Ramsay et al., 1985, J. Wildl. Dis. 21: 396–400). The advantage of this combination is a smooth induction and recovery due to the pressor and cataleptic effects of ketamine HCl being ameliorated by the sedative and myorelaxing effects of xylazine HCl (Amend, 1972, Vet. Med. Small Anim. Clin. 67: 1305–1307). The disadvantage of this combination is an extended recovery or prolonged sedation, usually attributed to xylazine HCl (Parry et al., 1981, op. cit.; Hatch et al., 1982, Am. J. Vet. Res. 43: 1009–1014; Ramsay et al., 1985, op. cit.).

The indolealkylamine, yohimbine HCl, has been used to antagonize xylazine HCl–ketamine HCl anesthesia in ungulates (Jessup et al., 1983, J. Am. Vet. Med. Assoc. 183: 1339–1340; Jacobson and Kollias, 1984, Proc. Am. Assoc. Zoo Vet., p. 57; Kitzman et al., 1984, Am. J. Vet. Res. 45: 875–879; Mech et al., 1985, J. Wildl. Dis. 21: 405–410; Jacobson et al., 1985, J. Am. Vet. Med. Assoc. 187: 1195–1198) and at least one wild carnivore (Ramsay et al., 1985, op. cit.). This paper reports on the use of yohimbine HCl to antagonize xylazine HCl–ketamine HCl anesthesia of coyotes (*Canis latrans* Say).

One adult male and four juvenile (two female, two male) wild-caught coyotes from South Dakota and one adult wild-caught female from Minnesota were used in this study. The five South Dakota coyotes were housed in indoor-outdoor pens at the Minnesota Zoological Gardens, Apple Valley, Minnesota. The Minnesota coyote was housed in an outdoor kennel approximately 80 km north of the other coyotes. The zoo coyotes were fed a commercial canine formulation once a day (Nebraska Brand, Central Nebraska Packing Inc., North Platte, Nebraska 69101, USA). The adult female was fed dry dog food ad libitum (Purina Brand Dog Chow, Ralston-Purina Co., St. Louis, Missouri 63178, USA). All coyotes were provided water ad libitum.

In October 1985, all coyotes were secured in a hand-held net and immobilized with a single, hand-injected, intramuscular dose of 2.0 mg/kg xylazine HCl (Rompun®, Haver-Lockhart Laboratories, Shawnee, Kansas 66201, USA), 4.0 mg/kg ketamine HCl (Ketaset®, Bristol Labora-

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tories, Syracuse, New York 13201, USA), and 0.02 mg/kg atropine sulfate (Atropine Injectable, S.A., Fort Dodge Laboratories, Inc., Fort Dodge, Iowa 50501, USA). Upon induction, all coyotes were placed in right lateral recumbency with heart rate, respiratory rate, rectal temperature, and capillary refill being monitored throughout the immobilization period. Approximately 20 min was allowed to elapse, then all coyotes received 0.2 mg/kg yohimbine HCl (Sigma Chemical Co., St. Louis, Missouri 63178, USA) administered via the cephalic vein. Yohimbine HCl was constituted at a concentration of 1.0 mg/ml in sterile 0.9% sodium chloride solution. Sterility of this solution was verified by inoculating on blood and MacConkey agar and incubating at 37 C for 24 and 72 hr. Arousal time (AT) and walk time (WT) was recorded on all animals. AT was the time for yohimbine HCl injection to when the animal opened its eyes and raised its head; WT was the time from yohimbine HCl injection to when the animal could walk in a directed manner of its own accord. One mo later, all the coyotes received the same anesthetic doses, administered in the same manner, but were allowed to recover on their own. Thus, each animal served as its own control. Statistical analysis was by one-way ANOVA. Means are reported with standard deviations.

The mean induction times (time from initial injection to immobilization) were 7.3 ± 3.9 min (range = 4–13 min) for the first trial and 7.0 ± 3.0 min (range = 3–11 min) for the second trial. There was no significant difference between these two times ($P \geq 0.86$). The time from induction to injection of yohimbine HCl was 20.2 ± 11.5 min (range = 11–39 min). The mean AT and WT for coyotes reversed with yohimbine HCl were 8.2 ± 5.4 min (range = 2–18 min) and 13.2 ± 7.7 min (range = 7–19 min). The total immobilization time (time from immobilization to ambulation) for coyotes receiving yohimbine HCl (33.3 ± 9.0 min; range = 21–46 min) was significantly less than the control times (70.5 ± 5.9 min; range = 61–77 min) ($P < 0.01$).

Within 5 min of receiving yohimbine HCl, the adult male coyote developed a fixed behavior pattern characterized by mouth gaping and face scratching with both forepaws. This behavior lasted approximately 10 min. One juvenile female also demonstrated unusual post-reversal behavior consisting of rhythmic, side-to-side head twitching and hyperreflexia. This behavior lasted for almost 35 min. Neither of these behavior patterns were observed when the animals recovered without yohimbine HCl.

Xylazine HCl is an alpha$_2$-adrenergic agonist that produces sedation and analgesia by stimulating central presynaptic adrenoceptors. This stimulation inhibits the influx of calcium during an action potential to prevent norepinephrine release at the nerve terminal (Starke, 1977, Rev. Physiol. Biochem. Pharmacol. 77: 1–124; Langer, 1981, Pharmacol. Rev. 32: 337–362). Yohimbine HCl is an alpha$_2$-adrenergic antagonist (Goldberg and Robertson, 1983, Pharmacol. Rev. 35: 143–180) that has been shown to reverse xylazine HCl-induced blockade of neural transmission in several species (Hsu and Shulaw, 1984, J. Am. Vet. Med. Assoc. 185: 1301–1303; Hatch et al., 1985, Am. J. Vet. Res. 46: 371–375).

The definitive site of action for ketamine HCl remains to be determined. Cholinergic (Leeuwin et al., 1984, Br. J. Pharmacol. 82: 339–347), serotonergic, gamma-aminobutyric acid, dopaminergic (Wright, 1982, J. Am. Vet. Med. Assoc. 180: 1462–1470), sigma opioid (Smith et al., 1980, Anesthesiology 53: 35) and N-methylaspartate (Thomson et al., 1985, Nature 313: 479–481) receptors have all been implicated as sites of action. Besides adrenergic activity, yohimbine HCl may

be capable of influencing cholinergic (Zetler and Thorner, 1973, Pharmacology 10: 238–251), serotonergic (Sanghvi and Gershon, 1970, Eur. J. Pharmacol. 11: 125–129), and dopaminergic (Scatton et al., 1980, J. Pharmacol. Exp. Ther. 215: 494–499) receptors. Thus, there may be some interaction between ketamine HCl and yohimbine HCl at common receptor sites.

The ability of yohimbine HCl to antagonize ketamine HCl anesthesia is equivocal. Domestic cats anesthetized with ketamine HCl (20.0 mg/kg), then given yohimbine HCl (0.25 mg/kg), had significantly shorter arousal times than did controls, but walk times were unchanged, or even lengthened (Hatch et al., 1983, Am. J. Vet. Res. 44: 417–423). Yohimbine HCl (0.5 mg/kg) failed to reverse ketamine HCl (10.0 mg/kg) anesthesia in rhesus monkeys (*Macaca mulatta*) (Lynch and Line, 1985, Lab. Anim. Sci. 35: 417–418) as well as in wolves (*Canis lupus* L.) (Kreeger and Seal, 1986, J. Wildl. Dis. 22: 600–603). Yohimbine HCl could be acting as a general stimulant to either reverse or override at least some of the effects of ketamine HCl (Hsu and Lu, 1984, J. Am. Vet. Med. Assoc. 185: 886–888). Thus, reversal of xylazine HCl–ketamine HCl anesthesia is probably due primarily to the antagonism of xylazine HCl by yohimbine HCl. The fixed behavior pattern observed in the two coyotes could be due to a residual ketamine HCl effect unmasked after antagonism of xylazine HCl.

The drug doses used in this study were an attempt to diminish the possible residual effects of ketamine HCl after yohimbine HCl reversal. Many anesthetic protocols have xylazine HCl–ketamine HCl ratios of 1:5 or higher (Stephenson et al., 1978, Vet. Med. Small Anim. Clin. 73: 303–305; Cornely, 1979, J. Wildl. Manage. 43: 577–578; Green et al., 1981, Lab. Anim. 15: 163–170; Moreland and Glaser, 1985, Lab. Anim. Sci. 35: 287–290). Our 1:2 xylazine HCl–ketamine HCl ratio reduced the amount of ketamine HCl required for immobilization and resulted in uncomplicated recoveries in four of six coyotes.

Atropine sulfate was included in this drug protocol to preclude any xylazine HCl-induced bradycardia (Klide et al., 1975, Am. J. Vet. Res. 36: 931–935).

Even though inductions were fairly quick and smooth, it should be remembered that these animals were caged and not overly stimulated prior to immobilization. Coyotes chased, or otherwise greatly excited, would be expected to require higher immobilizing doses (Nielson et al., 1982, op. cit.).

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