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XYLAZINE AND KETAMINE-INDUCED GLYCOSURIA IN WHITE-TAILED DEER

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ABSTRACT: This study documents glycosuria effects of xylazine and ketamine in eight captive and 19 free-ranging white-tailed deer (*Odocoileus virginianus*) from January to April 1985. Mean urinary glucose:creatinine ratios in two groups of deer fed high protein-high energy and low protein-low energy diets and in free-ranging deer were 1,000, 719, and 259, respectively. Glucose did not occur in urine of deer immobilized by physical restraint. Glucose:creatinine increased with the time interval between xylazine injection and urine collection in the two groups of captive deer.

Key words: Glycosuria, ketamine, *Odocoileus virginianus*, urinary glucose, white-tailed deer, xylazine.

INTRODUCTION

Xylazine (2(2,6 dimethylphenylamino)-4H-5,6-dihydro-1,3-thiazine hydrochloride) is a non-narcotic compound that has been increasingly used to immobilize white-tailed deer (*Odocoileus virginianus*) (Presnell et al., 1973; Roughton, 1975; Mautz et al., 1980; Warren et al., 1981; Mech et al., 1985; Kreeger et al., 1986a) and other wildlife species (Bauditz, 1972; Jessup et al., 1983; Herbst et al., 1985; Seal et al., 1985). Xylazine has analgesic, sedative and muscle relaxation effects (Bauditz, 1972; Thurmon et al., 1978; Raptopoulos and Weaver, 1984) and is often used effectively in combination with ketamine (Jessup et al., 1983; Mech et al., 1985).

Glucose is not present in urine of normal animals, but when the glucose load in blood exceeds the renal threshold, glycosuria occurs (Coles, 1980). Xylazine-induced hyperglycemia and hypoinsulinemia have been thoroughly documented in domestic cattle (Symonds and Mallinson, 1978; Eichner et al., 1979; Gorewit, 1980; Hsu and Hummel, 1981). Thurmon et al. (1978) demonstrated glycosuria and diuretic effects of xylazine in cattle. Evidence indicates that ketamine may induce mild increases in blood glucose of sheep; however, values remain below those necessary for glycosuria to occur (Kumar et al., 1974; Coles, 1980).

Hyperglycemia has been reported in captive white-tailed deer immobilized with xylazine (Mautz et al., 1980). However, effects of xylazine on urinary glucose of deer have not been reported. Herein, we document the effect of xylazine-ketamine immobilization of captive and free-ranging white-tailed deer on urinary glucose.

MATERIALS AND METHODS

Eight (five females, three males) captive white-tailed deer were individually confined in outdoor enclosures (15.5 × 30.0 m) in Grand Rapids, Minnesota, as part of a nutrition study. Four deer (two females, two males) were fed a high protein-high energy (HPHE, 11.1% crude protein [CP], 2,990 kcal digestible energy [DE]/kg) commercial, pelleted feed (E. J. Houle, Inc., 55 S.W. Second Street, Forest Lake, Minnesota 55025, USA) ad libitum, and four deer (three females, one male) were fed a low protein-low energy (LPLE, 6.3% CP, 1,995 kcal DE/kg) feed. The amount of feed provided to the latter group did not exceed mean consumption of the HPHE-fed group. Treatment diets were fed from 10 January to 5 April 1985.

Deer were anesthetized six times at 2-wk intervals from 24 January to 5 April 1985 between 0800 and 1200 hr. Deer were injected intramuscularly (i.m.) via pole syringe with a combination of 100 mg xylazine (Rompun, Haver-Lockhart Laboratories, Shawnee, Kansas 66201, USA) and 300 mg ketamine (Ketaset, Bristol Laboratories, Syracuse, New York 13201, USA) (Kreeger et al., 1986a). Supplemental i.m. in-

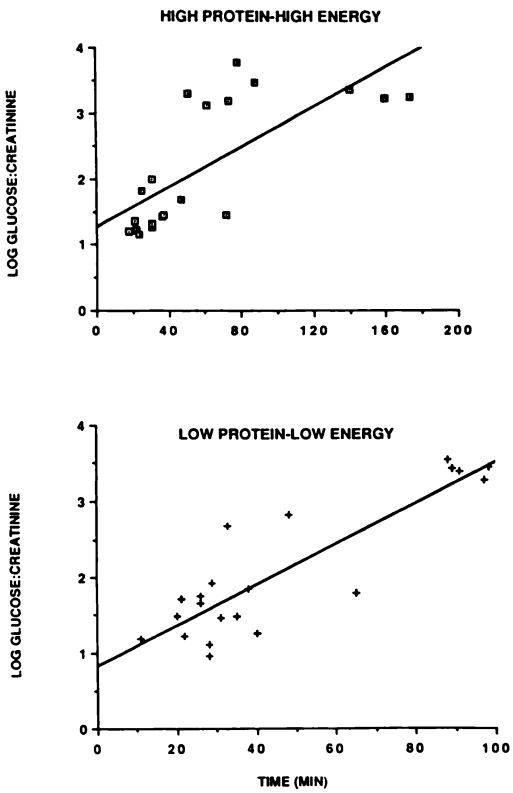

FIGURE 1. Relationships between log urinary glucose : creatinine and time between xylazine-ketamine injection and urine sampling of white-tailed deer fed high protein-high energy ($Y = 1.295 + 0.015x$, $R^2 = 0.54$, $P < 0.005$) and low protein-low energy diets ($Y = 0.854 + 0.027x$, $R^2 = 0.77$, $P < 0.005$).

jections of 200–900 mg of ketamine were administered only to maintain anesthesia. While immobilized, urine was collected via catheterization or cystocentesis (Kreeger et al., 1986b; DelGiudice et al., 1987). Deer also were weighed and blood samples taken from the jugular vein. Various doses of tolazoline (Kreeger et al., 1986a) or 15 mg of yohimbine (Mech et al., 1985) were injected intravenously to reverse immobilization.

Although a control group was not available during this study, a group of seven captive deer (five females, two males) that were immobilized by physical restraint and urine-sampled in a similar previous study, provided control values for urinary glucose (Seal, unpubl. data).

Nineteen free-ranging white-tailed deer (13 females, six males) were captured in clover traps (Clover, 1954) or rocket nets (Wildlife Materials, Inc., RR 1 Giant City Road, Carbondale, Illinois 62901, USA) from 18 January to 29 March 1985 in northeastern Minnesota. These deer were also immobilized with a combination of xlyazine (50–100 mg) and ketamine (300 mg). However, these deer were physically restrained while the xylazine-ketamine combination was administered i.m. with a hand-held syringe.

Urine samples were stored at −20 C and subsequently thawed and assayed spectrophotometrically for glucose (Barthelmai and Czok, 1962) and creatinine (Jaffe, 1886). Because single urine samples were assayed, data comparisons were made as glucose : creatinine ratios.

Data analysis for captive deer groups were made by 2-way analysis of variance (Hintze, 1982; Ott, 1984). Regression analyses were conducted according to Ott (1984). Data are presented in the text as means ± standard error of the means. The minimum acceptable significance level was $P \leq 0.05$.

RESULTS AND DISCUSSION

There were no differences in mean body weights, drug doses, or time intervals between the two captive deer groups (Table 1). Mean body weight, ketamine dose and time interval of the free-ranging deer were similar to those of the captive deer groups (Table 1). However, the mean xylazine dose administered to the free-ranging deer was less ($P < 0.001$) than that for both captive deer groups.

Glycosuria occurred in all chemically immobilized captive and free-ranging deer. There were no differences between the HPHE- and LPLE-fed deer for urinary glucose : creatinine, and ratios did not differ among sampling dates. Overall mean glucose concentrations for the HPHE and LPLE groups and free-ranging deer were 491 ± 157, 254 ± 65, and 100 ± 17 mg/dl; whereas, glucose : creatinine ratios were 1,000 ± 332, 719 ± 246, and 259 ± 101 mg/dl. There was no glucose in the urine of the physically restrained control deer. Similarly, urine tested negative for glucose in 67 undrugged, free-ranging white-tailed deer in Texas (Hoff and Trainer, 1975).

There were significant relationships between urinary glucose : creatinine and time interval in the HPHE ($Y = 1.295 + 0.015x$, $R^2 = 0.54$, $P < 0.005$) and LPLE-fed deer ($Y = 0.854 + 0.027x$, $R^2 = 0.77$, $P < 0.005$) (Fig. 1), but not in the free-ranging deer.

TABLE 1. Mean body weights, drug doses, and time intervals for captive and free-ranging deer in northern Minnesota, January–April 1985.[a]

Deer group[b]	n	Body weight (kg)	Xylazine dose (mg/kg)	Ketamine dose (mg/kg)	Time interval[c] (min)
HPHE	20	63.2 ± 1.3[d]	1.55 ± 0.03	4.6 ± 0.12	60.9 ± 8.9
LPLE	21	62.8 ± 2.2	1.63 ± 0.05	4.9 ± 0.15	45.9 ± 6.2
Free-ranging	19	65.5 ± 2.2	1.10 ± 0.09[e]	4.7 ± 0.50	49.4 ± 8.2

[a] Data were collected from the captive deer at 2-wk intervals; however, since no differences occurred between groups or among sampling dates, data were pooled.
[b] HPHE (fed high protein-high energy) and LPLE (fed low protein-low energy).
[c] Time interval between injection of the xylazine-ketamine combination and urine collection.
[d] Standard error of the means.
[e] Significantly ($P < 0.001$) different from the HPHE and LPLE groups.

Mautz et al. (1980) observed a linear increase in blood glucose of deer for 40 min postimmobilization with xylazine. The lower mean glucose:creatinine and absence of increasing ratios over time postinjection in our free-ranging deer may be attributable to the lower xylazine doses received or may reflect their existence at a lower nutritional plane with less readily available or circulating glucose (Beitz and Allen, 1984).

Thurmon et al. (1978) demonstrated similarly that glycosuria occurred in cattle given 0.22 or 0.44 mg/kg of xylazine, but it did not occur in control animals. Glucose appeared sooner and was detectable for a greater time in urine of cattle injected with the greater xylazine dose. Our deer were injected with xylazine doses greater than twice those used by Thurmon et al. (1978).

Although ketamine has negligible effects on blood glucose (Hsu and Hembrough, 1982; Hellgren et al., 1985) in monogastrics, it has induced mild hyperglycemias in domestic sheep (Kumar et al., 1974). However, values remained within the normal range for sheep (Coles, 1980) and below their renal threshold (Coles, 1980). Although excitement and restraint may also contribute to hyperglycemia (Mautz et al., 1980), glycosuria did not occur in physically-restrained control deer that were highly excitable during handling. Furthermore, induction time (interval between initial injection and immobilization) in the present study was generally <15 min (Kreeger et al., 1986a), but in the captive deer which received the larger xylazine doses the glucose:creatinine ratios increased with time postinjection beyond 150 min.

Xylazine is an alpha$_2$-adrenergic agonist (Doxey and Roach, 1980). Evidence from a study of xylazine-induced hyperglycemia in cattle (Hsu and Hummel, 1981) indicates that the glucose increase and associated hypoinsulinemia are mediated primarily by alpha$_2$-adrenergic receptors in beta-cells of pancreatic islets resulting in inhibition of insulin secretion. Increased hepatic glucose production may also contribute to the glucose increase in blood and urine (Hsu and Hummel, 1981).

Study of the potential of urinary characteristics as nutritional and health indices for deer has recently increased (Warren et al., 1981; 1982; Waid and Warren, 1984; DelGiudice et al., 1987; 1988). There are many diseases (hyperthyroidism, chronic liver disease, renal disease) that may cause glycosuria (Coles, 1980). Thus, for an accurate assessment of deer condition, it is important to be aware of the effects of xylazine on blood and urinary glucose. The present study demonstrates that glycosuria may be expected in deer immobilized with a xylazine-ketamine combination during seasons when forage protein and digestible energy levels are relatively high, as well as when they are diminished.

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