IMMOBILIZATION OF WILD DOGS (LYCAON PICTUS) WITH A TILETAMINE HYDROCHLORIDE/ZOLAZEPAM HYDROCHLORIDE COMBINATION AND SUBSEQUENT EVALUATION OF SELECTED BLOOD CHEMISTRY PARAMETERS

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IMMOBILIZATION OF WILD DOGS (*LYCAON PICTUS*) WITH A TILETAMINE HYDROCHLORIDE/ZOLAZEPAM HYDROCHLORIDE COMBINATION AND SUBSEQUENT EVALUATION OF SELECTED BLOOD CHEMISTRY PARAMETERS

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ABSTRACT: A tiletamine hydrochloride/zolazepam hydrochloride combination was used successfully to immobilize captive untamed wild dogs (*Lycaon pictus*) ($n = 16$) at dosage rates ranging from 2.3 to 32.3 mg/kg. Animals remained immobilized for periods ranging from 35 min to 24 hr 14 min. There was a significant positive correlation ($r = 0.85$, $P < 0.01$) between dosage rate and the time immobilized. Profuse salivation and intermittent mild myoclonal contractions were observed in some wild dogs. Mildly reduced partial oxygen and carbon dioxide pressures as well as reduced concentrations of bicarbonate were observed in arterial blood at 10 and 20 min after administration of the drug. Serum concentrations of sodium, potassium, chloride, phosphorus, calcium, magnesium, urea, creatinine, glucose, proteins, albumin, gammaglutamyltransferase, creatinine kinase, aspartate transaminase, alkaline phosphatase, lactate dehydrogenase, insulin, cortisol and thyroxine are presented. These concentrations were found to be in agreement with values previously reported for wild dogs.

Key words: Tiletamine hydrochloride, zolazepam hydrochloride, wild dog, *Lycaon pictus*, chemical immobilization, serum chemistries.

INTRODUCTION

Tiletamine hydrochloride, a cataleptoid or dissociative anaesthetic, in combination with zolazepam hydrochloride, a diazepinone tranquilizer, has been used extensively in the restraint and anaesthesia of a variety of exotic animal species (Bush and Custer, 1980; Boever et al., 1977). Tiletamine hydrochloride produces, depending on the dosage rate, deep analgesia and cataleptoid anaesthesia. The palpebral, corneal and swallowing reflexes remain intact, the eyes usually remain open and varying degrees of increased muscle tone are induced. The combination of tiletamine with zolazepam has reduced the tendency of tiletamine to induce convulsions. Depending on the dose, prolonged recovery periods may occur (Bree et al., 1972; Boever et al., 1977). Therefore, it may be inappropriate to extrapolate recommended dosages for domestic dogs to exotic carnivores when these dosages may result in highly undesirable prolonged recovery periods.

The wild dog (*Lycaon pictus*) is an endangered canid in the Republic of South Africa (Smithers, 1986). Therefore, safe chemical immobilization of this species becomes critically important. Wild dogs have been successfully immobilized with ketamine hydrochloride (Van Heerden and De Vos, 1981) and phencyclidine (Ebedes and Grobler, 1979). Inadequate muscle relaxation, convulsions and prolonged recovery periods are probably the most common untoward clinical side effects of these drugs in the wild dog. Thus, there is a need for a safe drug or drug combination which would result in rapid immobilization with adequate muscle relaxation. A relatively short recovery period is also desirable under field conditions. The aim of this investigation was to evaluate the effect of different dosage rates of a tiletamine/zolazepam combination in wild dogs. We also investigated serum concentrations of the more common blood chemistry parameters routinely used in the diagnosis of dis-

TABLE 1. Sex, body mass, dosage of tiletamine/zolazepam combination, time to sternal or lateral recumbency and time to recovery in immobilized wild dogs.

Animal number	Sex	Body mass (kg)	Dosage (mg/kg)	Time to sternal or lateral recumbency (min)	Time to recovery (min)
1	m*	19.0	2.7	3	43
2	m	20.5	2.5	4	45
3	m	17.5	2.9	7	42
4	f	20.0	3.8	0.5	88
5	m	21.0	6.0	2	197
6	f	19.0	13.2	1	292
7	f	24.0	10.4	3	319
8	m	21.0	19.0	2	1,298
9	m	20.0	25.0	2	1,454
10	f	15.5	32.2	2	756
11	f	20.0	2.6	4	45
12	m	20.5	2.9	2	65
13	m	22.0	2.3	4	57
14	m	17.0	2.9	5	54
15	m	17.5	2.9	4	63
16	f	17.0	2.9	5	35

* m, male; f, female.

ease conditions in canines, in these immobilized animals.

MATERIALS AND METHODS

Captive untamed male (n = 10) and female (n = 6) wild dogs (Numbered 1–16) with body masses ranging from 15.5 to 24.0 kg (Table 1) were immobilized with a tiletamine/zolazepam combination (Zoletil 100, Reading, Z.A.C. 17, rue des Marronniers, 94240 L'Hay-les-Roses, France), which contains 250 mg of tiletamine and 250 mg of zolazepam per ml, at dosages ranging from 2.3 to 32.3 mg/kg. The animals were held in enclosures in natural veld at a farm for the breeding of endangered species (27°55'S; 25°37'E; De Wildt Research Centre, De Wildt, Republic of South Africa). The animals appeared to be in good health and all, except Number 3, were in good physical condition. The cause of the relatively poor condition of Number 3 was not known. After being starved for at least 18 hr, 10 dogs were darted (Tel-in-ject, P.O. Box 2377, Randburg 2125, Republic of South Africa) one at a time, between 08:54 and 14:07 on an overcast day. The remaining six dogs were darted between 10:00 and 12:00 on another occasion.

Darted dogs were closely observed until they were mobile again. Adverse reactions as well as the time lapse between darting and sternal or lateral recumbancy and the time lapse between darting and recovery were recorded. Recovery was defined as the time when the dog was able to stand on all four legs. Female animals were subjected to a surgical incision of the skin, subsequent subcutaneous implantation of a slow-release progesterone preparation (Ulysses S. Seal, Research Service, Veteran's Administration Medical Centre, Minneapolis, Minnesota 55417, USA) and subcutaneous administration of an antibiotic (Compropen, Milborrow, Milborrow Animal Health, P.O. Box 27236, Benrose 2011, Republic of South Africa).

The pulse and respiratory rates as well as the rectal temperature were recorded 10 min after darting. Venous blood was collected in evacuated tubes (Vac-U-Test, Radem Laboratory Equipment, 704 6th Street, Wijnberg, Sandton, Republic of South Africa) from the *vena cephalica antebrachii* 10 min after darting. Arterial blood specimens were collected in heparinised syringes from the femoral artery 10 and 20 min after darting and stored on ice in a cool bag for approximately 2 hr prior to analysis of the blood by means of a fully automated blood gas analyzer (ABL3, Radiometer A/S Copenhagen, Denmark DK-2400).

Clotted blood specimens and blood collected in sodium fluoride/potassium oxalate tubes (Vac-U-Test, Radem Laboratory Equipment, 704 6th Street, Wijnberg, Sandton, Republic of South Africa) were delivered to the laboratory within 2 hr where the following assays were done: A continuous flow analyzer (SMA II Technikon Instruments Corporation, Tarrytown, New York 10591, USA) was utilized for the determination of sodium (Na), potassium (K), chloride (Cl), inorganic phosphorus (In. PO4), urea, creatinine, total protein and albumin. Except for Na and K, colorimetric methods were used for all above mentioned assays. Plasma glucose concentrations were determined with a discrete analyzer (Astra 8, Beckman Inc., Brea, California 92621, USA) which employs the glucose oxidase method. Total serum calcium and magnesium concentrations were determined with an atomic absorption spectrophotometer (Perkin-Elmer 5500, Perkin-Elmer Corp. Analytical Instruments Norwalk, Connecticut 06856, USA) utilizing an air-acetylene flame and a 0.16% (w/v) lanthanum oxide solution as diluent. The activities of gammaglutamyltransferase (GGT), creatine kinase (CK), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and lactate dehydrogenase (LD) were measured at 30 C with a Flexigem centrifugal analyzer (Electro-Nucleonics Inc., Fairfield, New Jersey 07006, USA) using Gemini® reagents kits (E. Merck, Darmstadt for Electro-Nucleonics Inc.). Serum tetraiodothy-

ronine (T4) and cortisol concentrations were determined with a radioimmunoassay (RIA) technique using Gamma Coat® [^{125}I] (Clinical Assays, Baxter Healthcare Corporation, Dade Division, Cambridge, Massachusetts 02139, USA) total T4 and cortisol reagent kits respectively. Serum insulin was determined by RIA utilizing a double antibody solid phase technique (Phadeseph®, Pharmacia Diagnostics AB Uppsala, S-71103 Uppsala, Sweden).

Time to sternal or lateral recombency and time to recovery were examined by regression analysis against dose rate. Variables of blood gas analysis obtained at 10 and 20 min after administration of the drug were compared by paired variate analysis. All laboratory variables as well as pulse rate, heart rate and rectal temperature, were examined by regression analysis against drug dose.

RESULTS

Approach to wild dog enclosures resulted in general excitement (evidenced by running and vocalisation) among the animals. Darting of each dog resulted in renewed excitement. In one animal, Number 3, spontaneous vomition and subsequent eating of the vomitus approximately 0.5 hr prior to immobilization was observed.

The dosage of the drug combination and time lapses to sternal recumbency or lateral recumbency and recovery are given in Table 1. Increased dosages of the drug in general resulted in decreased time to sternal or lateral recumbency, although this was found not to be statistically significant. Increased dosages were significantly associated with increased immobilization times ($r = 0.85$; $P < 0.01$). Dog Number 4 which was immobilized within 0.5 min, had accidentally been darted in the chest.

The mean pulse and respiratory rates as well as the mean rectal temperatures recorded were 156 per min (SD 45, range 80 to 240); 50 cycles per min (SD 29.4, range 20 to 140) and 39.2 C (SD 0.9, range 37.9 to 40.8), respectively.

Despite immobilization and excellent muscle relaxation (13 of 16 dogs), wild dogs immobilized with lower dosages (2.3 to 2.9 mg/kg) had intact flexor withdrawal reflexes and could still lift their heads. Profuse salivation occurred in 50% of the animals and intermittent mild myoclonal contractions occurred in Numbers 8 and 9. The bitches showed no reaction to surgical incision of the skin, implantation of progesterone preparations and subcutaneous administration of antibiotics.

The results of blood chemical and gas analyses are given in Table 2. Serum analysis of Number 3 yielded a very high insulin concentration of 54.3 mU/1. Dogs that were very exited and ran excessively prior to darting had relatively high serum cortisol concentrations (7.2 to 10.4 μg%). Examination of these laboratory variables by regression analysis against drug dosage failed to reveal any significant correlations. There was no statistically significant differences between blood gas variables recorded at 10 and 20 min after administration of the drug.

DISCUSSION

Parenteral administration of tiletamine hydrochloride and zolazepam hydrochloride at total dosage rates (equal concentrations) varying from 2.3 to 32.3 mg/kg resulted in rapid immobilization in all wild dogs. Compared to domestic dogs, where a dosage of 7.0 to 25.0 mg/kg is recommended by the manufacturer, wild dogs appeared to be more susceptible to the immobilizing effects of the drug combination.

Observed pulse rates for all dosage rates were within acceptable range. Increases in pulse rate during the first hour following administration of the drug combination has been reported in domestic dogs and cats (Tracy et al., 1988; Genevois et al., 1988) and has also been observed in ostriches (*Struthio camelus*) (J. van Heerden, unpubl. data). Lack of continuous monitoring of this and other parameters in fact reflects on a serious shortcoming of our investigation.

The considerable variation in respiratory rate was not significantly related to dosage rate of the drug, but is most probably primarily due to running and excitement prior to drug administration. The

TABLE 2. Concentrations of some serum chemical variables from wild dogs (n = 16) immobilized with tiletamine hydrochloride/zolazepam hydrochloride.

Parameter	$\bar{x}$	SD	Range
Sodium (mEq/l)	154	2.29	150–157
Potassium (mEq/l)	4.01	0.31	3.7–4.7
Chloride (mEq/l)	119.4	1.75	115–128
Phosphorus (mg%)	3.57	0.26	2.33–4.96
Calcium (mg%)	9.50	0.32	8.96–10.12
Magnesium (mEq/l)	1.70	0.10	1.58–1.86
Urea (mg%)	58.57	13.59	37.8–92.4
Creatinine (mg%)	1.08	0.22	0.7–1.44
Glucose (mg%)	118.68	22.42	82.8–160.2
Total proteins (g%)	5.5	0.28	5.2–6.0
Albumin (g%)	3.1	0.21	2.7–3.4
Gammaglutamyltransferase (U/l)	5	2.18	2–9
Creatine kinase (IU/l)	137	86.72	52–331
Aspartate transaminase (U/l)	35	13.97	22–66
Alanine transaminase (U/l)	55	21.43	34–115
Alkaline phosphatase (U/l)	66	47.52	13–192
Lactate dehydrogenase (U/l)	170	70.28	66–309
T4 (μg%)	2.5	0.63	1.79–3.57
Insulin (mU/l)	15.6	8.52	7.5–34[a]
Cortisol (μg%)	7.76	1.72	5.54–10.33
PO_2 (mmHg)[b]	76.96	12.23	51.4–91.7
PCO_2 (mmHg)[b]	29.63	2.67	24.1–36.8
HCO_3 (mmol/l)[b]	16.82	0.98	14.9–18.8
pH[b]	7.37	0.04	7.27–7.43
pH[c]	7.38	0.03	7.3–7.44
PO_2 (mmol/l)[c]	83.06	11.25	62.4–98.4
PCO_2 (mmHg)[c]	29.82	3.05	23–36.9
HCO_3 (mmol/l)[c]	17.40	1.02	15.5–19.5

[a] Excluding an outlying value of 54.3.
[b] Blood gas analysis at 10 min after administration of the drug.
[c] Blood gas analysis at 20 min after administration of the drug.

varying degrees of excitement and associated running observed prior to administration of the drug make it impossible to relate respiratory and cardiac rates to different dosages of tiletamine/zolazepam. It also was impossible for obvious reasons to obtain pre-immobilization baseline values. However, the PaO_2 values were within ranges acceptable for anaesthetized animals which are not anaemic, are not shivering and have a normal cardiac output, breathing air (Prys-Roberts, 1974).

Despite reduced bicarbonate concentrations in all instances, the pH remained within acceptable levels for immobilized animals. Although pre-immobilization activities of the animals may have resulted in a metabolic acidosis, the observed drop in bicarbonate concentration and carbon dioxide partial pressure has also been reported in lions immobilized with the same drug (Bush et al., 1978).

The adequate muscle relaxation at especially the relatively higher dosage rates, makes the tiletamine/zolazepam combination an acceptable drug for surgical procedures. The relatively wide range in dosage tolerated in wild dogs, underscores the wide safety margin of this drug combination. However, the drug should preferably be used at the lowest possible dosage rate to ensure a relatively short recovery period. Prolonged recovery associated with copious flow and loss of saliva may result in serious dehydration and loss in bodytemperature, especially in animals with subclinical renal disease. Since this investigation the authors have lost a wild dog

that had received the drug combination at a dosage rate of 2.5 mg/kg. The dog showed no signs of recovery and died within hours of administration of the drug. A subsequent post mortem investigation revealed extensive renal pathology. Renal disease would imply delayed excretion and thus prolonged activity of the drug (Tracy et al., 1988).

Analysis of serum of the immobilized wild dogs, for parameters listed in Table 2, yielded results comparable to previously reported results obtained from wild dogs immobilized with ketamine hydrochloride (van Heerden, 1986). The relatively high serum cortisol concentrations are indicative of the level of excitement experienced by the animals prior to and during immobilization. The relatively high insulin concentration in one animal which was immobilized and bled shortly after intake of regurgitated food, probably reflects a postprandial insulin surge. Holste et al. (1989) demonstrated a rapid increase in plasma insulin, with maximal concentrations occurring 30 min after feeding, in domestic dogs fed a soft moist diet.

In conclusion, the tiletamine hydrochloride/zolazepam hydrochloride drug combination has been found suitable for the immobilization of captive wild dogs. The drug also does not appear to affect the concentration of the more common blood chemical parameters.

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