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THE ACID-BASE STATUS OF LIONS, *Panthera leo*, IMMOBILIZED WITH FOUR DRUG COMBINATIONS [1]

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Abstract: Fifty-eight immobilizations were conducted using 21 lions *(Panthera leo)* and 4 drug combinations. The combinations used were ketamine-phencyclidine-promazine, xylazine-phencyclidine-promazine, xylazine-ketamine-phencyclidine-promazine, and tiletamine-zolazepam.

All 4 combinations produced only insignificant alterations to the lions' acid-base balance during immobilization. Tiletamine-zolazepam-immobilized lions had rapid induction times, good muscle relaxation and freedom from convulsions. Lions immobilized with the other 3 combinations encountered long induction periods, muscle rigidity, vomiting, retching and convulsions.

INTRODUCTION

Dissociative anesthetics are the most widely used agents for the immobilization of African lions *(Panthera leo).* Among this group of drugs are phencyclidine, ketamine and tiletamine. All are cyclohexylamines that produce profound analgesia and in high dosages a state of cataleptoid anesthesia.[18] With their use the palpebral, corneal and swallowing reflexes remain intact and the eyes are usually open. All three agents increase muscular tone to varying degrees.

Phencyclidine hydrochloride was the first member of this group to be used for lion immobilizations,[3,5,8,9] and is a proven effective immobilizing drug in this species; however, it has two major disadvantages when used alone: (1) an overt tendency to produce convulsions and muscle fasciculations and (2) relatively long induction and recovery times. By combining phencyclidine with a suitable tranquilizer, such as promazine hydrochloride, the long induction times and the convulsion problem are somewhat resolved.[12] Ketamine hydrochloride is a derivative of phencyclidine that also has been shown effective in immobilizing lions.[17] It has a more rapid induction time and a shorter recovery period than its progenitor. In addition, convulsions are not observed as frequently with ketamine. A major disadvantage is the large volumes of the drug required. An analogue of ketamine, tiletamine hydrochloride has been used successfully in the immobilization of several species of wild felids.[1,2,7] Like ketamine, it has rapid induction and recovery times. Additionally, it is a more potent drug than ketamine and, thus, requires smaller volumes to produce comparable effects. Tiletamine alone shows a proclivity for convulsions similar to phencyclidine. However, when combined with zolazepam, a diazepinone tranquilizer, in a 1:1 mixture, this tendency dis-

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appears. Thus, the tiletamine-zolazepam combination is the form of most common use.[4,13,16] Xylazine hydrochloride is a non-narcotic sedative and analgesic that is employed widely in the immobilization of ungulates. Its use in carnivores has been limited to domestic dogs and cats due to inadequacies found when used alone in larger wild animals. In this study, it was used in combination with the other drugs.

MATERIALS AND METHODS

The adult lions involved in this study form part of the pride of King's Dominion, Lion Country Safari, Doswell, Virginia. Fifty-eight immobilizations involving 21 individual lions were conducted using 4 drug combinations. The drugs used in the study were phencyclidine,[5] promazine,[6] ketamine,[7] tiletamine-zolazepam[8] and xylazine.[9] These agents were combined and used as follows: ketamine-phencyclidine-promazine (KPP) for 13 lions; xylazine-phencyclidine-promazine (XPP) for 19 lions; xylazine-ketamine-phencyclidine-promazine (XKPP) for 14 lions; and, tiletamine-zolazepam (TZ) for 12 lions. Some of the lions received different combinations on separate occasions.

The weights of the lions were estimated prior to injection and the drug dosages administered accordingly. In some instances, it was necessary to supplement the initial dosage to achieve the desired effects. During immobilization, the lions were weighed for actual dosage calculations. On some occasions, weights were calculated by obtaining girth measurements and applying appropriate regression equations.[11] For male lions the equation was: y (weight in kg) = -189.9 + 2.95 (girth in cm). For females the equation was: y (weight in kg) = -82.5 + 1.84 (girth in cm).

The drugs were administered to the caged lion with either a CO_2 pistol,[10] a syringe pole or by blowgun. Induction times were recorded as the length of time between injection and the time when the head was down and the animal was workable.

Arterial blood gas samples were collected approximately 30 min. after injection of the immobilizing agents. The sampling time varied with the length of the induction period. The sample was drawn anaerobically with a 1-ml sodium heparinized plastic disposable syringe and, after thorough mixing, introduced into a pH/blood gas analyzer.[11] Values for pH, pCO_2 and pO_2 were recorded at the instrument's temperature of 37 C. If not immediately analyzed, the sample was placed in an ice bath and analyzed within three hours. Respiration rate, pulse and rectal temperature were measured at the time of the arterial sampling. Subsequent arterial samples were drawn during the immobilizations and handled in a similar manner.

Values for pCO_2 and pO_2 were corrected to correlate with the animals' rectal temperatures using line charts prepared for dogs and man.[15] The pH values were corrected by adding or

[5] Sernylan, Bio-Ceutic Laboratories, Inc., St. Joseph, Missouri

[6] Sparine, Wyeth Laboratories, Inc., Philadelphia, Pa.

[7] Ketaset, Bristol Laboratories, Div. of Bristol-Myers Co., Syracuse, NY

[8] Telazol, Parke-Davis & Co., Ann Arbor, Michigan

[9] Rompun, Haver-Lockhart Laboratories, Div. of Bayvet Corporation, Shawnee, Kansas

[10] Cap-Chur Gun, Palmer Chemical & Equipment Company, Inc., Douglasville, GA

[11] IL Model 213 pH/Blood Gas Analyzer, Instrumentation Laboratories, Inc., Lexington, Mass.

subtracting 0.0147 pH units for each 1 C difference below or above, respectively, the instrumental temperature of 37 C.[10] The temperature-corrected values were then used to estimate base excess (BE) on an alignment nomogram.[14]

RESULTS AND DISCUSSION

The immobilizing dosages of all drug combinations used are listed with their mean induction times (Table 1). In general, the phencyclidine and promazine dosages were constant in the three combinations involving that pair. The xylazine dosages were also similar in the two combinations using that drug. Two lions in the XPP group received significantly ($p < 0.01$) higher dosages of all three drugs than did the other members of that group. The ketamine dosages were significantly ($p < 0.01$) higher in the XKPP group than they were in the KPP group of immobilized lions.

The group of lions immobilized with tiletamine-zolazepam had a mean induction time of 10.7 minutes. This short time contrasted sharply with the longer periods found in the other groups. The three combinations containing phencyclidine and promazine had mean induction periods of 23.5-24.9 minutes. The two lions in the XPP group that received higher dosages had a mean induction time of 9.5 minutes.

The arterial blood gas values obtained from initial samples during immobilization with all four drug combinations are presented (Table 2). The pH values of the TZ group were higher than the pH values found for the other groups. The difference was significant ($p < 0.01$) between the TZ group and the XPP group, but a wide variation of values prevented the determination of statistically significant differences between any other groups.

The mean pCO_2 values ranged 25.0-27.8 mm Hg and the mean pO_2 values ranged 104.9-114.6 mm Hg for the four groups. The mean BE values ranged -10.5 to -13.4. There were no significant differences determined for these values between the different drug combinations.

The low pH and negative base excess values indicated that the lions immobilized with any of the four drug combinations were experiencing a metabolic acidosis. However, the lower than normal pCO_2 and high pO_2 values indicate that there was some respiratory compensation for this acidosis. Subsequent arterial samples obtained during the immobilizations were very similar to these initial samples. The respiratory compensation precluded any significant alterations to the lions' acid-base balance that would have resulted from the metabolic acidosis.

The mean rectal temperatures, pulse and respiration rates measured approximately 30 min. after drug administration, at the time of arterial sampling, are tabulated (Table 3). The mean respiration rates of the four drug-immobilized groups ranged 13-21 breaths/minute; the mean rectal temperatures ranged 37.6-38.5 C. There were no significant differences for these measures between any of the immobilization groups. The mean pulse rates of the XPP and XKPP groups, however, were significantly ($p < 0.01$) lower than the other two groups' pulse rates. The two xylazine-containing groups had mean pulse rates of 50-59 beats/minute; the TZ- and KPP-immobilized lions had means of 100-107 beats/minute. Xylazine has known cardiovascular-depressant effects whereas dissociative agents are known to increase heart rate.[6] It appears that the effects of xylazine more than offset those of the dissociative agents in those lions immobilized with xylazine-containing combinations.

TABLE 1. Immobilizing dosages and induction times for lions immobilized with four drug combinations.

		DOSAGES (mg/kg)					
Drug Combination	Number	Ketamine	Xylazine	Phencyclidine	Promazine	Tiletamine-Zolazepam	Induction Time (Min.)
KPP	13	.82 ± .20*	—	.72 ± .12	.67 ± .15	—	24.6 ± 11.6
XPP	17	—	.37 ± .06	.64 ± .10	.64 ± .13	—	24.9 ± 18.3
	2	—	.96 ± .18	1.12 ± .02	1.10 ± 0.0	—	9.5 ± 0.7
XKPP	14	1.18 ± .08	.33 ± .09	.74 ± .13	.73 ± .32	—	23.5 ± 16.0
TZ	12	—	—	—	—	3.76 ± .48	10.7 ± 3.1

*All values — Mean ± S. D.

TABLE 2. Blood gas values of first arterial samples from lions immobilized with four drug combinations.

Drug Combination	Number	pH	pCO_2 (mm Hg)	pO_2 (mm Hg)	BE
TZ	12	7.35 ± .03*	26.3 ± 2.3	106.7 ± 20.6	-10.5 ± 2.6
KPP	13	7.30 ± .06	27.8 ± 4.7	114.6 ± 14.6	-11.6 ± 3.2
XPP	19	7.29 ± .02	25.0 ± 5.0	110.2 ± 10.5	-13.4 ± 2.7
XKPP	14	7.30 ± .11	27.6 ± 3.8	104.9 ± 12.8	-11.7 ± 5.0

*All values — Mean ± S. D.

TABLE 3. Physiological data of lions immobilized with four drug combinations.

Drug Combination	Number	Respiration Rate (Breaths/min)	Pulse (Beats/min)	Rectal Temp. (C)
TZ	12	21 ± 9*	100 ± 17	37.6 ± 1.2
KPP	13	13 ± 5	107 ± 17	37.8 ± 0.7
XPP	19	21 ± 10	59 ± 19	38.5 ± 1.0
XKPP	14	18 ± 11	50 ± 12	38.3 ± 1.0

*All values — Mean ± S. D.

The most undesirable side effect of phencyclidine use is its strong tendency to produce convulsions and muscle fasciculations. Therefore, it has become customary to combine phencyclidine with the tranquilizer, promazine, to reduce its convulsive activity. In this study, four different chemical combinations were used to immobilize lions, three of which contained the phencyclidine-promazine combination. Convulsions were observed in all three of these groups. Lions immobilized with the fourth combination, tiletamine-zolazepam, had no convulsions in twelve episodes (Table 4).

In all three groups with convulsive activity, the dosages received by the lions with convulsions were similar to those dosages received by the non-convulsing lions. The lone exceptions to this were two lions, in the XPP group, that received significantly ($p < 0.01$) higher dosages of all three drugs than the other lions immobilized by that combination. These two lions had convulsions that were more frequent and more prolonged than those seen in other members of that, or any other, group.

Total mean dosages of 0.65 - 0.85 mg/kg body weight of phencyclidine, and similar total dosages of promazine, were used in all three groups using that combination (Table 4). At those dosages, the tendency toward convulsions probably relied upon other factors as well as the phencyclidine-promazine levels. Seal and Erickson[12] used dosages of 0.7-1.5 mg/kg body weight of phencyclidine and promazine to immobilize lions, observing only one episode of convulsions in 32 immobilizations.

The percentage of lions with convulsions in the KPP and the XKPP groups were 15.4% and 57.1%, respectively. A comparison of the dosages used in these two combinations

TABLE 4. Total dosages administered to convulsing and non-convulsing lions immobilized with three drug combinations.

Drug Combination	Number	DOSAGES (mg/kg) Ketamine	Xylazine	Phencyclidine	Promazine
KPP					
Convulsing	2	.73 ± .02*	—	.84 ± .08	.85 ± .16
Non-Convulsing	11	.83 ± .21	—	.70 ± .12	.65 ± .14
XPP					
Convulsing	4	—	.43 ± .04	.75 ± .18	.80 ± .20
Convulsing	2	—	.96 ± .16	1.12 ± .03	1.10 ± .02
Non-Convulsing	13	—	.38 ± .07	.65 ± .11	.63 ± .12
XKPP					
Convulsing	8	1.14 ± .15	.35 ± .08	.83 ± .30	.76 ± .18
Non-Convulsing	6	1.23 ± .11	.30 ± .04	.72 ± .09	.76 ± .30

*All values — Mean ± S. D.

revealed that significantly ($p < 0.01$) higher ketamine dosages were used in the XKPP group. The xylazine dosages in the XKPP group were similar to those used in the XPP group, in which 23.5% of the lions receiving those dosages had convulsions. Whether the increased convulsive activity in the XKPP group could be attributed to the higher ketamine dosages alone was not clear, since the possibility of interactions between ketamine and other members of the combination cannot be overlooked.

Elevated temperatures were observed during one immobilization with each of the XPP, XKPP and TZ combinations. The temperatures peaked at 41.3, 41.3 and 40.1 C, respectively, for the three groups. A relationship between these temperature peaks and convulsive activity in those groups could not be determined.

Vomiting and retching were observed in 4 of 17 lions immobilized with the lower dosages of the XPP combination. These four lions received dosages similar to the other lions in that group.

Tiletamine-zolazepam proved to be the most desirable immobilizing combination for lions in this study. It provided rapid induction times, freedom from convulsions and sufficient muscle relaxation for electroejaculation, blood collection and electrocardiography. Convulsions, long induction periods, vomiting and retching were problems encountered with the other combinations using phencyclidine, promazine, ketamine and/or xylazine.

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