

KETAMINE AND KETAMINE:XYLAZINE ED₅₀ FOR SHORT-TERM IMMOBILIZATION OF THE ISLAND FLYING FOX (*PTEROPUS HYPOMELANUS*)

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Abstract: Ketamine and a combination of ketamine and xylazine were evaluated for short-term restraint of adult island flying foxes (*Pteropus hypomelanus*). Although both regimens provided effective immobilization, the ketamine:xylazine combinations produced better-quality induction, immobilization, and recovery with less struggling and biting than ketamine alone. Induction times were similar for several regimens and dosages. The effective dosages (ED₅₀) for ketamine and ketamine:xylazine for ≥ 30 min of immobilization were approximately 34 and 9:1.8 mg/kg, respectively. A ketamine:xylazine dosage of 10.0:2.0 mg/kg produced a mean immobilization time of 38 ± 8 min. At all dosages, bats administered ketamine alone had higher heart and respiration rates 10 or more min after drug administration than with ketamine:xylazine.

Key words: Ketamine, xylazine, island flying fox, *Pteropus hypomelanus*, bat.

INTRODUCTION

Island flying foxes (*Pteropus hypomelanus*) belong to a family (Pteropodidae) of medium to large exclusively Old World fruit- and nectar-feeding bats, many species of which are either threatened or endangered.⁵ Physical restraint of these large bats during field research is difficult and dangerous. Consequently, short-term chemical restraint is indicated in many species for nonsurgical procedures (e.g., morphometry, phlebotomy). However, there is limited published information on parenteral anesthetic regimens in bats.¹ In two species of 7–14-g mouse-eared bats (*Myotis lucifugus* and *M. sodalis*), ketamine alone (120 mg/kg i.m.) produced anesthesia for 20–30 min.³ A combination of acepromazine (1.1 mg/kg) and ketamine (11 mg/kg) has been reported to effectively immobilize Indian flying foxes (*P. giganteus*).¹ Ketamine and xylazine (dosages not given) were successfully used for immobilization of grey-headed (*P. poliocephalus*), black (*P. alecto*), and little red (*P. scapulatus*) flying foxes during electrophysiologic studies.⁶ This study evaluated ketamine and ketamine:xylazine dos-

ages for short-term immobilization of medium to large flying foxes.

MATERIALS AND METHODS

Animals

Seven (three males, four females; ≥ 2 yr old; 558 ± 32 g) island flying foxes (*Pteropus hypomelanus*) were used. This study was approved by the Institutional Animal Care and Use Committee at the University of Florida, Gainesville, Florida, USA. Each bat was assessed to be healthy based on a physical examination and hematologic and plasma biochemical values that tested within normal reference ranges for the collection. All bats were group-housed in indoor/outdoor enclosures at the Lube Foundation, a private breeding and research facility in north-central Florida. Each bat was exposed to a natural photoperiod, received a mixture of fruits, vegetables, and commercial primate diets and received water ad libitum.

Drugs

Commercial preparations of ketamine HCl (100 mg/ml; Ketaset, Fort Dodge Laboratories Inc., Fort Dodge, Iowa 50501, USA) and xylazine (20 mg/ml; Rompun 20, Miles Agricultural Division, Shawnee Mission, Kansas 66216-1846, USA) were used. Equal volumes of ketamine and xylazine

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were combined within 3 hr of use to make a concentration of 50 and 10 mg/ml, respectively. All bats randomly received each of four dosages of ketamine alone (30, 32.5, 35, and 37.5 mg/kg) and ketamine:xylazine (5:1, 7.5:1.5, 10:2, and 12.5:2.5 mg/kg). A minimum of 5 days was allowed between successive drug treatments. All drug doses were administered into the pectoral muscle mass with a 0.5-ml insulin syringe and 25-ga needle.

Experimental protocol

The bats were transported to the University of Florida on the morning of the study and returned the same day. All bats were caged in a quiet room for at least 2 hr before handling, then placed in a pillow case, weighed, and administered the calculated dose. After injection each bat was held upside down by its feet until nystagmus was observed, then placed in dorsal recumbency on a warming water blanket. A lead II electrocardiogram was continuously monitored on an oscilloscope (Datascop 870, Data-scop Corporation, Paramus, New Jersey 07652, USA) and used to obtain heart rate. Respiration rate was determined by observation of thoracic movement. Respiration and heart rates were recorded every 5 min for as long as immobilization allowed. At the lower dosages heart and respiration rates were not recorded at all times because of struggling. Palpebral response was assessed by gently touching the medial canthus of the eye. Biting response was evaluated by placing a pen at the commissure of the mouth.

Induction time was defined as the period between injection and loss of the righting response. Immobilization time was defined as the time elapsed from induction to the return of righting response. Return of righting response was assessed to be when the bat was able to turn over onto its ventrum within 2 min. Following return of the righting response, each bat was returned to its holding cage. When necessary, bats were wrapped in a towel to prevent them from

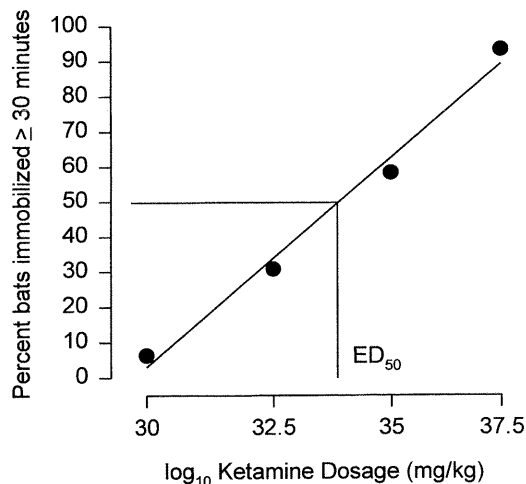


Figure 1. Graph of \log_{10} ketamine dosage vs. percentage of animals immobilized. This graph was used to determine effective dosage (ED_{50}) for short-term immobilization (≥ 30 min) of seven island flying foxes (*P. hypomelanus*).

flapping and injuring their wings until they were able to hang unassisted from the cage ceiling.

Determination of effective dosage

The ED_{50} was determined from the plots as the drug dosage at which 50% of bats were immobilized for ≥ 30 min. Dose response curves were plotted as \log_{10} dose (mg/kg) vs. the percentage of bats immobilized ≥ 30 min for this purpose (Figs. 1, 2).

Statistical analysis

An analysis of variance for repeated measures was used to compare variable response means between dosages. Where a significant effect was identified, Tukey's post hoc test was used to determine which means were different. In using this analysis we assumed that allowing at least 5 days between dosings minimized any interaction between successive dosages. Incomplete data sets were not included in the statistical analysis. A P value of ≤ 0.05 was considered significant.

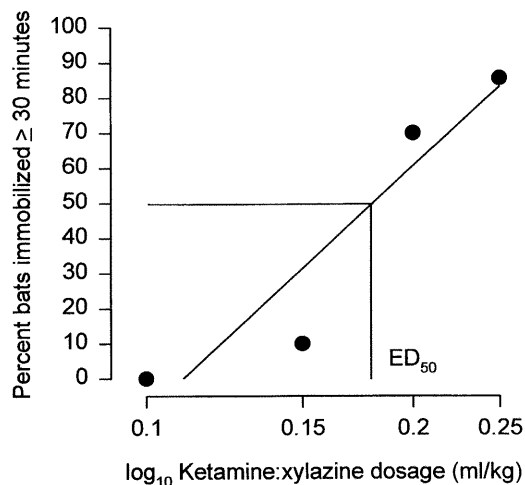


Figure 2. Graph of \log_{10} ketamine : xylazine dosage (ml/kg) vs. percentage of animals immobilized, this graph was used to determine effective dosage (ED_{50}) for short-term immobilization (≥ 30 min) of seven island flying foxes (*P. hypomelanus*). Equal volumes of commercial solutions of ketamine (100 mg/ml) and xylazine (20 mg/ml) were combined to produce a solution of 50 mg/ml ketamine and 10 mg/ml xylazine.

RESULTS

Induction times for the highest dosages of ketamine (37.5 mg/kg) and ketamine : xylazine (12.5:2.5 mg/kg) were 51 ± 15 and 93 ± 35 sec, respectively (Table 1). Mean induction and immobilization times did not differ significantly among ketamine dosages. The mean induction time for keta-

mine : xylazine 10.0:2.0 mg/kg (64 ± 9 sec) was significantly lower than for the 5.0:1.0 mg/kg dosage (103 ± 22 sec). The mean immobilization times for ketamine : xylazine 10.0:2.0 mg/kg (38 ± 8 min) and 12.5:2.5 mg/kg (39 ± 11 min) were significantly greater than for those at 5.0:1.0 mg/kg (14 ± 5 min) and 7.5:1.5 mg/kg (22 ± 8 min). The estimated ED_{50} for ketamine and ketamine : xylazine for ≥ 30 min of immobilization was 34 and 9:1.8 mg/kg (0.18 ml/kg), respectively (Figs. 1, 2).

Bats administered ketamine alone had significantly higher heart rates than when given ketamine : xylazine at all dosages (Table 2). Ten or more minutes after drug administration, flying foxes administered ketamine alone also had significantly higher respiration rates than when given ketamine : xylazine (Table 2). At all dosages, ketamine : xylazine immobilization produced less struggling, fewer muscle tremors, and longer sedation during recovery than ketamine alone. Following return of the righting reflex, ketamine : xylazine-immobilized bats could always be immediately returned to the recovery cage, where they would hang quietly from the cage ceiling without flapping or struggling. In contrast, ketamine-immobilized bats usually had to be wrapped in a towel during recovery to prevent injury from struggling and wing flap-

Table 1. Induction and immobilization times for intramuscular ketamine and ketamine : xylazine in seven adult island flying foxes (*P. hypomelanus*). Ketamine mean induction and immobilization times were not significantly different between dosages. The mean induction time for ketamine : xylazine 10.0:1.0 mg/kg was significantly lower than for 5.0:1.0 mg/kg. The mean immobilization times for ketamine : xylazine 10.0:2.0 and 12.5:2.5 mg/kg were significantly greater than for those at the lower dosages. A P value ≤ 0.05 was considered statistically significant. Mean \pm SD.

Drug regimen	Dosage (mg/kg)	Induction time (sec)	Immobilization time (min)
Ketamine	30.0	52 ± 11	28 ± 6
	32.5	42 ± 5	31 ± 5
	35.0	51 ± 17	33 ± 7
	37.5	51 ± 15	38 ± 5
Ketamine : xylazine	5.0:1.0	103 ± 22	14 ± 5
	7.5:1.5	94 ± 12	22 ± 8
	10.0:2.0	64 ± 9	38 ± 8
	12.5:2.5	93 ± 35	39 ± 11

Table 2. Effects of i.m. ketamine and a ketamine:xylazine combination on heart and respiratory rates in seven adult island flying foxes (*P. hypomelanus*). ND = either not determined or incomplete data. At all dosages, bats administered ketamine alone had significantly higher heart rates ($p \leq 0.05$) than with ketamine:xylazine. Bats administered ketamine alone had significantly greater respiration rates at all dosages at ≥ 10 min than with ketamine:xylazine. Mean \pm SD.

Drug	Dosage (mg/kg)		Time					
			5 min	10 min	15 min	20 min	25 min	
Ketamine	30.0	HR ^a	259 \pm 70	302 \pm 45	317 \pm 35	335 \pm 31	ND ^b	
		RR ^c	76 \pm 29	80 \pm 31	ND	ND	ND	
	32.5	HR	244 \pm 34	268 \pm 28	306 \pm 42	327 \pm 39	ND	
		RR	75 \pm 23	102 \pm 34	ND	ND	ND	
	35.0	HR	249 \pm 29	261 \pm 36	295 \pm 35	328 \pm 23	ND	
		RR	76 \pm 18	82 \pm 20	92 \pm 19	ND	ND	
	37.5	HR	257 \pm 18	ND	ND	335 \pm 50	338 \pm 44	
		RR	63 \pm 11	76 \pm 21	ND	ND	ND	
	Ketamine:xylazine	5.0:1.0	HR	ND	ND	ND	ND	ND
			RR	78 \pm 30	ND	ND	ND	ND
7.5:1.5		HR	185 \pm 22	179 \pm 15	182 \pm 14	ND	ND	
		RR	51 \pm 16	59 \pm 4	65 \pm 9	ND	ND	
10.0:2.0		HR	184 \pm 14	168 \pm 12	160 \pm 12	158 \pm 14	151 \pm 12	
		RR	46 \pm 5	53 \pm 16	46 \pm 9	58 \pm 18	53 \pm 16	
12.5:2.5		HR	202 \pm 17	188 \pm 19	174 \pm 15	173 \pm 19	171 \pm 20	
		RR	54 \pm 22	55 \pm 19	57 \pm 10	53 \pm 18	ND	

^a HR = heart rate, beats/min⁻¹.

^b ND = not determined or incomplete data.

^c RR = respiratory rate, breaths/min⁻¹.

ping. The palpebral reflex was not obtunded by either drug regimen at any dosage. Although not quantitated, the return of a biting response appeared to occur earlier in the immobilization period with ketamine than with ketamine:xylazine. Bats often had to be restrained during ketamine recovery to prevent them from biting and injuring their first phalanx.

DISCUSSION

Both ketamine and ketamine:xylazine produced effective short-term immobilization in these flying foxes. However, the ketamine:xylazine combinations produced better-quality induction, immobilization, and recovery. Xylazine decreased muscle tone and the amount of ketamine required and also produced sufficient sedation in the recovery period to keep the bats quiet without wing flapping until they were fully recovered. The effects of xylazine observed in these bats are the same as those reported for other mammalian species.²

The technique of probit analysis^{4,7} was not used in this study for determination of the ED₅₀ because most of the values for percentage of bats immobilized were either ≥ 0 or ≤ 100 . The use of only four points in this study to calculate ED₅₀ is less than ideal. Similarly, the lack of a statistical difference for immobilization times among ketamine dosages weakens the ED₅₀ estimate. However, the study was designed only to approximate an appropriate immobilization dosage in these bats. The ketamine:xylazine ED₅₀ obtained in this study is similar to that for the ketamine dosage of 11 mg/kg, which is reported to be effective in the Indian flying fox when combined with acepromazine.¹ The apparent tachycardia produced by ketamine alone in this study of island flying foxes has also been reported in mouse-eared bats (*M. lucifugus* and *M. sodalis*) and other mammalian species.^{3,8} Similarly, bradycardia and bradypnea observed with the ketamine:xylazine combi-

nation has also been observed in other species.²

In conclusion, we recommend a ketamine:xylazine combination at a dosage of 10:2 mg/kg for short-term chemical immobilization of the island flying fox.

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