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Authors: Heard, Darryl, Towles, Jennifer, and LeBlanc, Dana

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Evaluation of Medetomidine/Ketamine for Short-term Immobilization of Variable Flying Foxes (*Pteropus hypomelanus*)

Darryl Heard,[1,3] Jennifer Towles,[1] and Dana LeBlanc[2] [1] Box 100126 HSC, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, Florida 32610-0126, USA; [2] The Lubee Bat Conservancy, Lacrosse, Florida 32609, USA; [3] Corresponding author (email: HeardD@mail.vetmed.ufl.edu)

ABSTRACT: Four medetomidine/ketamine (M/K) doses (30 μg/kg/3 mg/kg; 40/4; 50/5; 60/6), administered by intramuscular injection, were evaluated for short-term immobilization of adult male variable flying foxes (*Pteropus hypomelanus*). The highest dose (60 μg/kg/6 mg/kg) produced a significantly faster induction (31±46 sec) than the lowest dose (30/3) (125±62 sec). The highest dose levels (50/5, 60/6) produced significantly longer immobilization times (52.5±25.7 min and 60.6±20.8 min, respectively) than did the lower doses (30/3, 40/4) (18.8±8.7 min and 31.0±14.3 min, respectively). The dose at which 50% of the bats were immobilized for ≥30 min (ED_{50}) was approximately 40 μg/kg/4 mg/kg. This dose produced a mean immobilization time of 31±14 min, bradypnea and bradycardia. In conclusion, a M/K dose of 50 ug/kg/5 mg/kg is recommended for greater than 30 min of relaxed immobilization in free-living variable flying foxes and is sufficient for safe collection of samples.

Key words: Anesthesia, bat, flying fox, ketamine, medetomidine, *Pteropus hypomelanus*.

Although bats belong to the second most diverse mammalian order, Chiroptera, published information on anesthetic regimens in these animals is limited (Heard, 2003). The variable or small island flying fox (*Pteropus hypomelanus*) has the greatest distribution range of any member of its genus, extending from the Indo-Australasian Archipelago, Papua New Guinea, and Trobriand and Woodlark islands, westward to Thailand and the Mergui Archipelago, excluding Java and the lesser Sunda Islands (Jones and Kunz, 2000). Physical restraint of these and other medium to large Old World fruit bats may result in trauma to both handlers and bats. Flying foxes are also reservoirs for several zoonotic diseases transmitted by bites and aerosolization including henipaviruses and lyssaviruses (Heard, 2003). Short-term chemical restraint, therefore, is indicated to reduce injury and prevent disease transmission during restraint for examination, measurement, and sample collection. Although inhalation anesthesia is preferred because of rapid induction and recovery (Jonsson et al., 2004) it is impractical for field work in many areas where flying foxes live. Parenteral anesthetic techniques offer the advantages of minimal equipment and portability.

Although ketamine alone (34 mg/kg) produces chemical restraint, it is associated with poor relaxation and wing flapping during recovery (Heard et al., 1996). A xylazine (2 mg/kg)/ketamine (10 mg/kg) combination has been shown to provide high-quality, short-term immobilization of variable flying foxes (Heard et al., 1996). The potent and selective α_2-adrenergic agonist medetomidine potentiates ketamine (Moens and Fargetton, 1990) and may reduce its effective dose 75% or more than xylazine (Jalanka, 1989). Medetomidine/ketamine (M/K) combinations have been used in a variety of mammalian species (Jalanka, 1993), but their use in bats has not previously been reported.

All research was conducted at the Lubee Bat Conservancy, LaCrosse, Florida (29°41′N, 82°16′W) between June and September 1999. This study was preapproved by the University of Florida Institutional Care and Use Committee. Ten adult (>3 yr old), intact male variable flying foxes weighing 716±70 g (mean±1 SD) were used. The bats were housed in indoor/outdoor enclosures and exposed to a natural photoperiod. All received water ad libitum and were fed a mixture of fruits,

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vegetables, and commercial fruit bat supplement after dusk. Food and water were not withheld before immobilization. Before inclusion in the study, each bat was assessed to be healthy based on physical examination and hematologic and plasma biochemistry values were within established reference ranges (Heard and Whittier, 1997). A minimum of 3 days was allowed between each experiment and all were performed in the morning.

Immediately before each experiment equal volumes of medetomidine (1.0 mg/ml; Domitor, Pfizer Animal Health, Exton, Pennsylvania, USA) and ketamine (100 mg/ml; Ketaset, Fort Dodge Laboratories Inc., Fort Dodge, Iowa, USA) were combined into a solution with concentrations of 0.5 mg/ml and 50 mg/ml, respectively. All drugs were administered into the left pectoral muscle mass of the manually restrained bats using a 0.5-ml insulin syringe and 27-gauge needle.

All statistical analyses were performed using a commercial statistical program (Minitab Inc., State College, Pennsylvania). An analysis of variance for repeated measures was used to compare means. Where a significant effect was identified, Tukey's post hoc test was used to determine which means were different. It was assumed that allowing at least 3 days between experiments minimized any interaction between successive doses. A P value of ≤ 0.05 was accepted as significant.

The first experiment examined effectiveness of four M/K doses (30 μg/kg/3 mg/kg, 0.06 ml/kg; 40/4, 0.08; 50/5, 0.10 and 60/6, 0.12) to produce short-term immobilization. All 10 bats received each of the drug combination doses in random order. Following injection, each animal was held upside down by its feet and its righting response from dorsal recumbency was determined by laying the bat on a table every 10 sec. Palpebral response was assessed by gently touching the medial canthus. Biting response was evaluated by placing a plastic fecal loop at the commissure of the mouth. The clinch response was determined by placing the tool against the pad of the feet and assessing toe flexion. Induction time was defined as the period between drug injection and loss of the righting response. Immobilization time was defined as the time elapsed from induction to the return of the righting response. Return of the 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 placed in its holding cage and allowed to roost unassisted from the cage ceiling. The medetomidine was not reversed. The effective dosage$_{50}$ (ED_{50}) was defined as the drug dosage at which 50% of bats were immobilized for $\geq$30 min. This was determined by Probit analysis using a commercial graphing program (SigmaPlot 8.0, Systat Software, Point Richmond, California, USA) (Reed and Meunch, 1934; McGrath et al., 1984).

The second experiment evaluated the effects of a single M/K dose (40 μg/kg/4 mg/kg) on respiration and heart rates. Recordings were made before injection, and every 5 min for the first 15 min. The heart rate was determined by monitoring the audible pulse of a Doppler probe placed over a pedal artery. Respiration rate was assessed by observation of thoracic movement.

Induction and immobilization times were dose-dependent (Fig. 1). The highest dose (60 μg/kg/6 mg/kg) produced a significantly faster induction (31±46 sec) than the lowest dose level (30/3) (125±62 sec). The highest dose levels (50/5, 60/6) produced significantly longer immobilization times (52.5±25.7 min and 60.6±20.8 min, respectively) than the lower doses (30/3, 40/4) (18.8±8.7 min and 31.0±14.3 min, respectively). The estimated ED_{50} for M/K for $\geq$30 min of immobilization was approximately 40 μg/kg/4 mg/kg (0.08 ml/kg). The palpebral response was absent for only a short period of time

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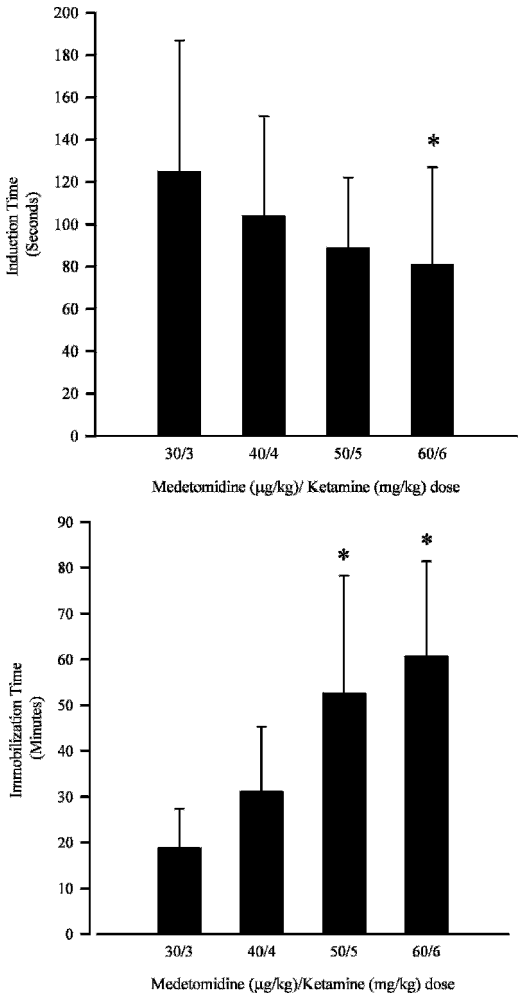


FIGURE 1. Induction and immobilization times (mean±1 SD) following intramuscular injection of medetomidine/ketamine combinations in adult, male, variable flying foxes (*Pteropus hypomelanus*) ($n=10$). * =significantly different ($P \leq 0.05$) from the lowest combination dose (analysis of variance for repeated measures and Tukey's post hoc test).

in one or two bats at the highest doses. At all doses the clinch reflex returned before biting (Fig. 2). The biting reflex was absent significantly longer with each increase in dose. The dose of 40 μg/kg/4 mg/kg induced a mild, but significant bradypnea (123±55 to 98±63 breaths/min) and bradycardia (239±37 to 191±32 beats/min) within 5 min of administration. All animals at all dose levels were completely recovered by 3 hr after drug administration.

All M/K doses used in this study produced effective short-term immobilization in these variable flying foxes similar to that reported in other mammalian species (Jalanka, 1993). When compared to using ketamine alone (34 mg/kg intramuscular [IM]) (Heard et al., 1996), medetomidine decreased muscle tone and reduced the amount of ketamine required to produce a similar period of immobilization almost sixfold. This reduction was greater than that produced by xylazine (2 mg/kg IM) (Heard et al., 1996).

During induction, the palpebral response was lost first, followed by clinch and biting responses (Fig. 2). These responses returned in the reverse order during recovery. The absence of a clinch response in an immobilized bat would, therefore, indicate that it is unlikely to bite. Conversely, the relatively early return of the clinch response allows a bat to be suspended in a cage before full recovery. Medetomidine produced sufficient sedation during recovery to prevent bats flapping their wings, as occurs when ketamine is used alone (Heard et al., 1996).

The clinical use of the ED_{50} dose would only produce effective short-term immobilization of 50% of the bats. It is, therefore, recommended that a M/K dose of 50 μg/kg/5 mg/kg be used clinically to produce at least 30 min of immobilization in all bats. The α_2-adrenergic antagonist atipamezole was not used to reverse the medetomidine in this study because it might have "unmasked" the adverse effects of the ketamine such as wing flapping. Further studies are indicated to determine whether medetomidine reversal will hasten recovery without adverse effects. All bats were completely recovered by 2–3 hr after initial drug administration. This would allow free-living bats captured between dusk and midnight to be released before dawn.

The physiologic monitoring in the study was limited. The observed mild to moderate bradypnea and bradycardia are

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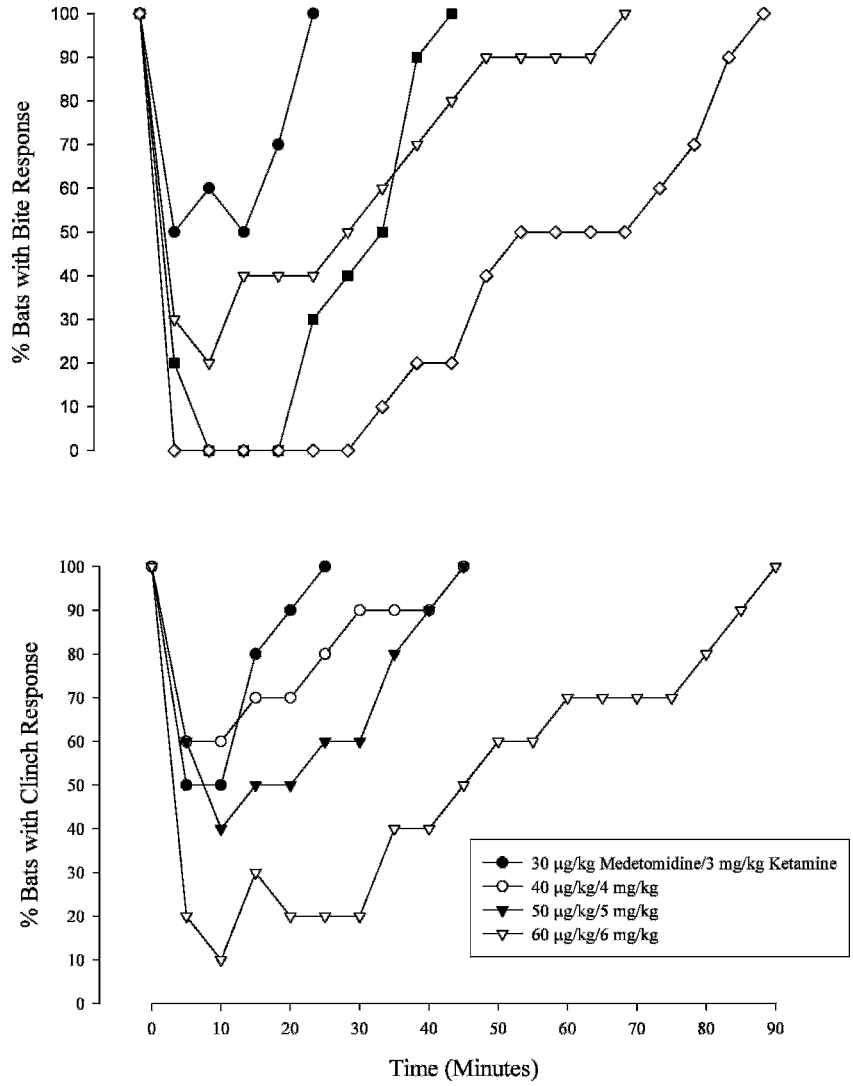


FIGURE 2. Percentages of variable flying foxes (*Pteropus hypomelanus*) ($n=10$) showing a bite or clinch response over time following four medetomidine/ketamine doses.

similar to that previously described in a variety of mammals (Moens and Fargetton, 1990; Jalanka, 1993; Dobronmylskyj, 1996). Although no mortality was associated with M/K administration in these bats, further studies to evaluate the cardiopulmonary effects of these drugs are recommended. Medetomidine alters cardiovascular function through its effects on both central and peripheral receptors (Cullen, 1996). Central receptor stimulation increases vagal tone and decreases sympathetic activity producing bradycardia and hypotension. Severe peripheral vasoconstriction makes interpretation of mucous membrane color difficult and results in hypertension with associated reflex bradycardia (Cullen, 1996).

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