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ANESTHESIA OF CAPTIVE AFRICAN WILD DOGS (*LYCAON PICTUS*) USING A MEDETOMIDINE–KETAMINE–ATROPINE COMBINATION

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Abstract: Seven captive male African wild dogs (*Lycaon pictus*) weighing 25–32 kg each, were anesthetized by i.m. injection via hand syringe with a combination of 1.5 mg/kg ketamine, 40 μg/kg medetomidine, and 0.05 mg/kg atropine. Following endotracheal intubation, each animal was connected to a bain closed-circuit system that delivered 1.5% isoflurane and 2 L/min oxygen. Atipamezole (0.1 mg/kg i.v.; 0.1 mg/kg i.m.) was given at the end of each procedure (60 min following injection of medetomidine/ketamine/atropine). Time to sternal recumbency was 5–8 min. Times to standing after atipamezole administration were 8–20 min. This anesthetic regimen was repeated on three separate occasions (September 2000, February 2002, and October 2002) on all males to perform electroejaculation procedures. Each procedure was <80 min from injection to standing. Dogs showed excellent muscle relaxation during the procedures. Arterial blood samples were collected at 10-min intervals for blood gases in one procedure (September 2000). Separate venous samples were taken from each dog during each procedure for hematology and biochemistry. These values were within the normal range for this species. Arterial hemoglobin oxygen saturation (SpO2) and heart rate (HR) were monitored continuously in addition to other anesthesia monitoring procedures (body temperature, respiratory rate [RR], capillary refill time, blink response, pupil position, deep pain perception reflex). All dogs maintained relatively stable SpO2 profiles during monitoring, with a mean (± SD) SpO2 of 92% ± 5.4%. All other physiological variables (HR, RR, body temperature, blood pressure) were within normal limits. Following each procedure, normal behavior was noted in all dogs. All the dogs were reunited into the pack at completion of their anesthetic procedures. An injectable medetomidine–ketamine–atropine combination with maintenance by gaseous isoflurane and oxygen provides an inexpensive, reliable anesthetic for captive African wild dogs.

Key words: African wild dog, anesthesia, atipamezole, ketamine hydrochloride, *Lycaon pictus*, medetomidine hydrochloride.

INTRODUCTION

The African wild dog (*Lycaon pictus*) is one of the most endangered carnivores in the world, with approximately 3,000 individuals left in Africa.[10] Many factors have contributed to their decline, including persecution by man, competition for prey with lions and hyena, diminishing habitat and range, and susceptibility to domestic dog diseases such as rabies and canine distemper.[10]

Captive populations of African wild dogs have been established for educational and research purposes with a view to aiding their survival in the wild. The establishment of a sound anesthetic protocol that could be adapted for use in the wild would reduce risks associated with handling of the animals for management or research purposes in African free-range situations.

Chemical anesthesia in the African wild dog has been reviewed.[4,15] This work suggested that alpha-2 adrenergic agonists (e.g., medetomidine–xylazine–detomidine) in combination with a dissociative anesthetic (e.g., ketamine–tiletamine–phencyclidine) provided the best anesthetic regimen for African wild dogs. The advantages of this combination are that 1) muscle rigidity, caused by the dissociative agent, is reduced by the alpha-2 agonist and 2) a specific alpha-2 antagonist (e.g., atipamezole) can be used to specifically reverse the effects of the alpha-2 agonist drug.

Medetomidine, ketamine, and atropine have been used extensively in domestic dogs and their cardiopulmonary effects have been studied.[6] In this study, a combination of medetomidine, ketamine, and atropine was used on seven captive male African wild dogs over three different time periods.

MATERIALS AND METHODS

Seven clinically healthy male African wild dogs, located at Western Plains Zoo (Dubbo, Australia) ranging in age from 18 mo to 4 yr with a mean

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bodyweight 29 ± 3.2 kg, were separated from the female(s) in the pack prior to each procedure. Each animal was anesthetized on three separate occasions to give 21 anesthetic observations. After restraining each animal in a purpose-built crush cage, each dog received a combination of ketamine hydrochloride (Ketamine injection®, 100 mg/ml; Parnell Laboratories (Australia) Pty Ltd, Alexandria, New South Wales 2015, Australia; 1.5 mg/kg, i.m.), medetomidine hydrochloride (Domitor®, 1 mg/ml, Novartis Animal Health Australasia Pty Ltd, North Ryde, New South Wales 2113, Australia; 0.04 mg/kg, i.m.), and atropine sulphate (Atropine injection®, 0.6 mg/ml, Apex Laboratories Pty Ltd, Somersby, New South Wales 2250, Australia; 0.05 mg/kg, i.m.) by i.m. injection into the left quadriceps muscle via a hand syringe. Anesthetic dose rate was based on previously determined body weights (measured on scales placed into a raceway) and an assessment of general body condition. Time from injection to sternal recumbency and immobility was noted.

Once the dog had fallen into lateral recumbency and was immobile, he was removed from the cage and transported to the Western Plains Zoo Veterinary Quarantine Centre (VQC) by stretcher. Upon arrival at the VQC, the animal was weighed and placed onto the treatment room table in right lateral recumbency. Each dog was intubated with a size 10 endotracheal tube and oxygen and isoflurane was administered via a circle absorber system. Anesthesia was maintained with 1.5 % isoflurane in 2 L/min oxygen during the entire procedure (from placement onto the treatment table to departure to enclosure). This level was adjusted to meet the needs of each individual dog. A sterile ophthalmic ointment (Lacrilube, Allergan Pharmaceuticals, Johannesburg, Republic of South Africa) was applied to the eyes of each dog prior to blindfolding to aid lacrimation. Catheters were inserted into the right cephalic vein and the right dorsal metatarsal artery. Venous blood samples were collected from the cephalic vein for hematology and biochemistry values. Arterial blood samples were assessed at 10-min intervals for blood gases (pH, pCO2, p_aO2, $HCO3^-$) in one of the three procedures (September 2000): 2-ml heparinized plastic syringes were used to slowly collect arterial blood. After collection, the syringe barrel was rotated to disperse heparin and allow air to collect at the liquid surface, facilitating gas expulsion. Air was expelled from the syringe and a rubber stopper was placed over the luer tip to maintain an anaerobic environment. The blood sample was placed into an ice container and analyzed for blood gases within 15 min at Orana Pathology (Orana Base Hospital, Dubbo, Australia).

Monitoring of anesthesia commenced upon removal of the animal from the cage and included continuous recording of pulse rate and hemoglobin oxygen saturation, using a pulse oximeter with the sensor placed onto each patient's tongue (Nellcor N-20P, Nellcor, Hayward, California 94545, USA), heart rate, respiratory rate, rectal temperature (pre- and postelectroejaculation), palpation of femoral pulse quality and regularity, muscle relaxation, mucous membrane color, and capillary refill times. Arterial blood pressure was measured on all dogs during one of the three anesthetic procedures (September 2000) indirectly via a ''Dinamap'' pressure monometer cuff (Dinamap Adult/Pediatric Vital Signs Monitor, Critikon Inc., Tampa, Florida, USA). During each period of anesthesia, electroejaculation (EJ) procedures were conducted. Semen was successfully collected from six dogs in one of the three procedures (February 2002). The EJ procedure involved electrical stimulus of the prostate and ductus deferens using a rectal probe. The EJ procedure was similar to that previously described[7], except that a Standard Precision Electronics stimulator (Model 524; Colorado, USA) was used; this stimulation unit produced a round square wave of approximately 22 Hz and had a maximum voltage output of 15 V. The EJ procedure was terminated after total stimulation time of 15 mins irrespective of whether semen was collected. This EJ method caused only mild transient elevations in heart rate, respiration rate and blood pressure.

Reversal of medetomidine hydrochloride was achieved by administering atipamezole hydrochloride (Antisedan®, 5 mg/ml, Novartis Animal Health Australasia Pty Ltd, North Ryde, New South Wales 2113, Australia; 0.1 mg/kg i.v. via right cephalic vein and 0.1 mg/kg i.m. via left cranial quadriceps muscle) 60 min after medetomidine–ketamine–atropine injection. Time to standing following atipamizole administration was recorded. Prior to reversal, meloxicam (Metacam®, Boehringer Ingelheim Animal Health Australasia Pty Ltd, North Ryde, New South Wales 2113, Australia; 0.2 mg/kg, s.c.), an anti-inflammatory agent, was administered and the intravenous and arterial catheters were removed. Each procedure lasted no longer than 80 min from initial injection to standing.

RESULTS

Central nervous system (CNS) depression was achieved in 5 ± 1.2 min after injection of medetomidine–ketamine–atropine. Lateral recumbency was achieved in 7 ± 1.4 min. Anesthesia was main-

Table 1. Anesthetic variables of African wild dogs using medetomidine–ketamine–atropine; bpm = beats per min; SpO2 = oxygen saturation.

Variable	Heart rate (bpm)	Respiration rate (bpm)	SpO2 (%)	Body temperature (°C)	Blood pressure (mmHg)
Mean	102 ± 17	24 ± 7.8	92 ± 5.4	39.0 ± 1.56	101 ± 8
Min	86 ± 24	18 ± 2.4	88 ± 4.2	37.8 ± 0.45	72 ± 9 (diastolic)
Max	124 ± 32	28 ± 3.2	97 ± 2.7	39.8 ± 1.20	140 ± 7 (systolic)

tained with isoflurane–oxygen for 35 ± 9.3 min. Each dog was administered isoflurane–oxygen after arrival at VQC. The duration of maintenance anesthesia was determined by the EJ procedures conducted on each dog. Total time for each procedure was no longer than 80 min.

The hematology and biochemistry results (Na^+, K^+, Cl^-, $HCO3^-$, anion gap, urea, creatinine, glucose, bilirubin, aspartate transferase (AST), alanine transferase (ALT), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), protein, albumin, globulin, calcium, phosphate, cholecytikinase, cholesterol, triglycerides) were within normal limits.[8,13] All dogs showed excellent skeletal muscle relaxation, pale pink oral mucous membranes, and normal capillary refill times. Rectal temperatures ranged from 39.5–41.0°C at initial handling. At the end of each procedure, rectal temperatures ranged from 37.8–39.7°C. Mean heart rates (HR), respiratory rates (RR), oxygen saturations (SpO2), rectal body temperatures (BT), and blood pressure (BP) values are presented in Table 1. Minimum and maximum values depict the range of each variable. All dogs showed initial relative bradycardia (70–85 beats per min [bpm]) after administration of the anesthetic combination and mild tachycardia during EJ stimulus (130–160 bpm). Respiratory rates were maintained within normal ranges (16–28 breaths/min). Arterial hemoglobin oxygen saturation (SpO2) readings were relatively stable for all dogs over all procedures. Medetomidine caused an initial decline to minimum SpO2 values, which improved over the duration of each procedure as a result of oxygen flow via circle absorber system. Maximum SpO2 values were achieved while maintenance isoflurane–oxygen anesthesia was given and following reversal of medetomidine with atipamizole.

Table 2. Arterial blood gas and electrolyte values of African wild dogs using medetomidine–ketamine–atropine.

Blood gas/electrolyte	Measured values (mean ± SE)	Reference values[14]
pH	7.30 ± 0.23	7.35–7.45
$HCO3^-$	23 ± 2.4 mmHg	24–25 mmHg
pO2	98 ± 4.2 mmHg	>90 mmHg
PCO2	49 ± 3.7 mmHg	35–45 mmHg
Anion gap	−2.8 ± 1.45 mmHg	−4 to 4 mmHg
K^+	4.8 ± 0.65 mmol/L	3.8–5.8 mmol/L
Na^+	145 ± 4.2 mmol/L	140–155 mmol/L

Arterial blood gas and arterial blood pressure measurements were only made on one occasion (September 2002). All arterial blood pressure measurements (taken during maintenance anesthesia) were within normal limits (Table 1). Arterial blood gas and electrolyte values (K^+, Na^+) were also in normal ranges (Table 2).[14] The dogs stood 16 ± 5.8 min (n = 21) following atipamezole administration with only mild signs of ataxia. All dogs recovered normally following each procedure and remained clinically healthy.

DISCUSSION

Anesthesia of wild dogs has improved significantly over the last decade with the advent of newer drugs with fewer side effects. Twenty free-ranging adult African wild dogs were successfully anesthetized in Botswana using a ketamine–xylazine–atropine combination.[5] Other drug protocols used for anesthesia of the African wild dog include medetomidine,[18] ketamine hydrochloride,[1] a fentanyl–droperidol–ketamine combination,[17] medetomidine–ketamine,[13,18] phencyclidine hydrochloride,[1,4] phencyclidine–promazine,[11,12] fentanyl–xylazine,[9,15] and tiletamine–zolazepam.[16] Free-ranging wild dogs have also been captured successfully without drugs using a helicopter-assisted boma technique.[2] A combination of medetomidine, ketamine, and atropine was used in this study to create a highly repeatable, inexpensive, reliable, safe anesthetic regimen for captive conditions when maintained with gaseous isoflurane–oxygen.

Ketamine is a rapid-acting general anesthetic with significant analgesic activity and a lack of cardiopulmonary depressant effects. It induces amne-

sia and anesthesia by functionally disrupting the CNS through overstimulation.[6] The dose of ketamine that produces anesthesia in dogs is very near to that which causes convulsions and hence this drug cannot be recommended as a sole agent for canine anesthesia.[6] Anesthesia with ketamine is characterized by excitement during induction, paddling of feet, poor muscle relaxation, excessive salivation, and violent and prolonged recoveries[6].

However, when an alpha-2 adrenergic agonist (e.g., medetomidine, xylazine) is combined with ketamine, the dose of ketamine needed to induce anesthesia is reduced. This also has the effect of reducing recovery time. The sedative and hypnotic effects of the alpha-2 adrenergic agonist have been shown to be synergistic with ketamine.[6] In addition, an alpha-2 adrenergic agonist increases the degree of muscle relaxation and smoothes the induction of anesthesia and recovery. Premature reversal of the alpha-2 adrenergic agonist will unmask the excitatory effects of ketamine and its active metabolites and may cause excessive stimulation of the CNS resulting in signs of excitement and ataxia. In this study, medetomidine was reversed with atipamizole at the end of each procedure 60 min following induction of anesthesia. The potential for these adverse effects is further reduced if the dose of ketamine is reduced. The low dose of ketamine used in this study may permit reversal of medetomidine at an earlier stage of anesthesia without evidence of ketamine-induced CNS stimulation.

The dosages used in the present study were similar to other studies using an alpha-2 adrenergic agonist–ketamine combination.[5,13] These dosages are significantly lower than those used in other studies of xylazine and medetomidine in free-range protocols.[16,18] This is not surprising, considering the African wild dogs at Western Plains Zoo were conditioned to human contact and were not as athletic as their wild counterparts. The seven dogs chosen for this study roam as a pack in a large, open exhibit but are relatively well habituated to keepers at Western Plains Zoo for feeding and routine veterinary procedures. Restraint of the dogs is relatively stress-free with a purpose-built cage constructed into the normal passageway by which the dogs access the exhibit. This restraint allowed a much smoother anesthetic induction than when xylazine–ketamine was administered by dart because of the precise placement of the anesthetic combination into the quadriceps muscles. The African wild dogs used in the free-range study in Botswana[5] had become ''habituated to humans'' suggesting these wild dogs responded similarly to captive dogs with respect to anesthetic dosages. In a free-range situation, where dogs are more excitable and aggressive than in the present study, higher doses of ketamine may be required.

Medetomidine is a potent, selective drug that produces a dose-dependent decrease and release of noradrenalin in the CNS manifested by sedation, analgesia, and bradycardia.[6] Medetomidine was preferred over xylazine for sedation because of its longer duration of action and reduced emetic effects.[6] In addition, yohimbine hydrochloride is only a partial antagonist of medetomidine and xylazine and hence recoveries would be expected to be substantially longer than following administration of the complete antagonist, atipamezole hydrochloride.[6] The operator has greater control over the anesthetic procedure if one of the drugs in the combination can be totally reversed should any detrimental effects be observed.

In our study, atipamezole was administered at five times the dose of medetomidine and divided into two portions for reversal, one given i.v to give immediate arousal of the animal, the other given i.m to provide sustained antagonism of residual medetomidine. Atipamizole was given 60 min following administration of the medetomidine–ketamine–atropine combination.

Atropine sulfate has been used extensively in domestic canid anesthesia for counteracting salivation induced by ketamine administration, and bradycardia effects of alpha-2 agonist drugs such as medetomidine and xylazine hydrochloride.[6] Usually, however, premedication is possible in domestic canids as opposed to nondomestic canids. A recent study[3] showed that atropine did not prevent hypertension-associated effects of medetomidine despite effectively preventing bradycardia. Atropine may contribute to hypertension in animals administered medetomidine by increasing heart rate through a constricted vascular system, thereby increasing cardiac output requirements (afterload). This may be avoided in future studies by the addition of acepromazine to reduce vasomotor activity and minimize the effects of medetomidine on bradycardia and afterload-induced hypertension. Ketamine dose levels may also be reduced with the addition of acepromazine to the combination. Because hypotension is the major detrimental effect of anesthetic agents, atropine administration was valid for this study to prevent medetomidine-associated bradycardia and ketamine-associated hypersalivation.

Following administration of medetomidine–ketamine–atropine by injection, there was sufficient sedation and relaxation of the laryngeal reflex to allow endotracheal intubation. Settings of 1.5% isoflurane in 2 L/min oxygen were maintained during

each procedure. These settings were based on eye position, strabismus, blink reflex, pinch reflex, and other anesthetic monitoring parameters.[6] Settings were adjusted according to the needs of each individual patient.

Continuous monitoring of arterial hemoglobin oxygen saturation (SpO2) via pulse oximetry allows field evaluation of drugs such as medetomidine that effect oxygen delivery. SpO2 values in this study were reduced by medetomidine, but were still within normal limits (>90%). Improved SpO2 values may be achieved using lower medetomidine doses (0.01 mg/kg) and higher ketamine doses (5 mg/kg) in future anesthesia trials. The addition of acepromazine to the combination will aid peripheral vasodilation and reduce afterload effects on the heart. The arterial blood pressure values all were within normal limits for domestic dogs. Alpha-2 adrenergic agonists have been well documented to reduce cardiac output and peripheral blood flow and patients given higher doses of medetomidine should be monitored very carefully.

This study involved three separate anesthetic procedures with the same seven male African wild dogs, giving highly repeatable data. There were no differences in responses to drugs or measurements taken between the three anesthesia periods. The anesthetic described in this study provided an inexpensive, consistent, reliable, and safe method of anesthetizing captive African wild dogs. This protocol has very short recovery times and repeatable data over different seasons.

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