Anaesthesia of roan antelope (*Hippotragus equinus*) with a combination of A3080, medetomidine and ketamine

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ABSTRACT

A dose range was determined for anaesthesia of 20 recently boma-captured roan antelope (*Hippotragus equinus*) with the synthetic opiate A3080 combined with medetomidine and ketamine. A dose of 10–30 μ/kg A3080 ($\overline{x} = 20 \pm 8$ μg/kg) combined with 5–21 μg/kg medetomidine ($\overline{x} = 13 \pm 7$ μg/kg) plus 0.29–1.11 mg/kg ketamine ($\overline{x} = 0.71 \pm 0.24$ mg/kg) was found to be safe and effective for the field conditions in this study. The anaesthesia produced by this drug combination was predictable and characterised by a short induction time, good muscle relaxation, and acceptable physiological parameters for anaesthesia periods ranging from 49–103 min ($\overline{x} = 64 \pm 19$ min). The wide range (3–4-fold) of doses with acceptable results is also an indication that this drug combination has a wide margin of safety in roan antelope, making it desirable for field use. When 2 dose levels (2–3-fold difference) were retrospectively evaluated, no statistical difference was found in induction times, and no observable clinical differences in the anaesthetic episodes were seen. Based on this study, the recommended dose range in roan antelope for this combination is 10–13 μg/kg A3080, 5–6 μg/kg medetomidine and 0.3–0.6 mg/kg ketamine. The anaesthesia produced by this combination was rapidly and completely reversed by i.m. or i.v. injections of naltrexone at 30 times the A3080 dose ($\overline{x} = 0.60 \pm 0.25$ mg/kg) and atipamezole at 3 times the medetomidine dose ($\overline{x} = 38 \pm 20$ μg/kg). No residual effects from ketamine were noted following reversal of A3080 and medetomidine. No mortality was associated with this protocol.

Key words: A3080, anaesthesia, atipamezole, *Hippotragus equinus*, ketamine, medetomidine, naltrexone, roan antelope.

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INTRODUCTION

The roan antelope (*Hippotragus equinus*) is rare throughout its range in southern Africa and is highly prized on game farms and in National Parks, which have ongoing conservation programmes to protect and propagate this species. Roan antelope are large, strong and aggressive, with curved horns and can be dangerous to handle if not properly anaesthetised[3]. There are several reports describing a variety of anaesthetic techniques used for roan antelope over the last 4 decades[3,5,11–14]. Neuroleptic-narcotic combinations have been the drugs of choice for field capture of roan antelope[3,13]. The current suggested protocol combines etorphine and a sedative/neuroleptic such as azaperone or xylazine[3]. The induction time reported with these combinations averages 7 min 36 sec, which can allow darted animals to range up to 5 km[5]. If induction is prolonged it may predispose to secondary hyperthermia and excessive muscle exertion[2,5], which can lead to capture myopathy. Once recumbent, roan antelope can be dangerous if semi-immobilised and may require supplemental anaesthetic before manipulation[3].

A3080 is a synthesised fentanyl derivative with rapid, pronounced opiate agonist activity. It has a much shorter duration of action than carfentanil or etorphine and is only slightly less potent than carfentanil[10,16,17]. A3080 shortens induction times over carfentanil in cervids by 26–65 %[10]. Induction times were dose-dependent in a study using A3080 in impala[7,8] and in another study using elk[10,17]. Narcotic antagonists such as naltrexone (NAL) provide rapid and complete reversal of A3080 with no reports of renarcotisation[8,10,16,17].

Medetomidine (MED) is an imidazole-based compound with potent selective and highly specific agonist activity at both pre- and post-synaptic alpha$_2$-adreno-receptors[18,19]. It has an alpha$_2$-binding affinity of 10 times that of the commonly-used sedative xylazine[6,18]. MED is a potent sedative and analgesic with anxiolytic properties[6,19], and, at high doses, it produces hypnotic or anaesthetic effects[19]. MED provides good muscle relaxation with minor physiological changes in Arabian oryx[4], and, when combined with ketamine (KET), is effective in a broad range of non-domestic ungulates[6]. The combination of KET and MED has a potentiating effect in carnivores[6]. Ketamine also potentiates synthetic opiates[15]. A combination of etorphine and MED provides adequate immobilisation of Arabian oryx for at least 3 h[1]. The potent and selective alpha$_2$-adrenoreceptor antagonist atipamezole (ATI) is highly effective in reversing sedation/anaesthesia induced by MED or MED-KET combinations[6,19].

The objective of this study was to determine whether the rapid induction potential of A3080 could be combined with the potent selective alpha$_2$-agonist effects of MED and the synergistic effects of KET to produce a predictable, rapid, balanced anaesthesia in roan antelope. It is suggested that the combination of A3080, MED and KET will produce a rapid, smooth induction in roan antelope followed by an anaesthetic period characterised by good myorelaxation and maintenance of physiological parameters within acceptable ranges, and be rapidly and completely reversed with NAL and ATI without the undesirable sequelae of repeated narcotisation or sedation.

MATERIALS AND METHODS

This study was conducted in September 1999 in the Kasungu National Park in Malawi. Twenty adult and subadult roan antelope (8 males, 12 females) were studied in a concurrent capture operation for their relocation to Liwonde National Park in Malawi. The roan antelope were herded into a capture boma by helicopter and allowed to calm down for several

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hours. All animals were in good physical condition, and their pelage and muscle mass was considered to be good for the season and available native vegetation. No obvious signs of disease were seen in the animals.

The anaesthetics used in this study were A3080 (10 mg/mℓ, Wildlife Pharmaceuticals, Karino), medetomidine hydrochloride (MED) (20 mg/mℓ, Wildlife Pharmaceuticals, Karino) and ketamine hydrochloride (KET) (200 mg/mℓ, Wildlife Pharmaceuticals, Karino) formulated as sterile injectable solutions in multi-dose vials. The doses of A3080, MED and KET were adjusted based on a visual evaluation of each animal's weight and success of previous anaesthetic procedures. The drugs were delivered by a CO_2-powered remote injection device delivering a 3-mℓ plastic air-pressurised dart with a 40 × 2 mm collared needle (Dan-Inject SA) to insure a deep intramuscular (i.m.) injection.

The entire capture operation, involving 20 roan antelope, was completed in 6.5 h. The darting was performed at night from outside the capture boma. Once an animal was recumbent and herd mates were separated into other compartments of the boma, it was carried to a central location for monitoring. Initial data collected included time from dart delivery to first signs of drug effect, the time from dart delivery to recumbency, and the time from recumbency to the start of physiological monitoring (lag time). Physiological data collected included heart rate, respiration rate, oxyhaemoglobin saturation (SpO_2), indirect arterial blood pressure (systolic, diastolic and mean), end tidal CO_2 ($ETCO_2$) and rectal temperature. Heart rate was determined by auscultation of the heart (verified by pulse oximeter and indirect blood pressure monitors), respiration rate by counting chest excursions (verified by $ETCO_2$ monitor), SpO_2 by the use of a portable pulse oximeter (Nellcor N-200®, Nellcor) with the sensor placed on a shaved portion of the ear or on the tongue. Indirect blood pressure was measured by the use of a portable blood pressure monitor (Dinamap Compact Monitor T®, Critikon) with the cuff placed on the metacarpus. $ETCO_2$ was measured using a handheld monitor (7000 Vet/Cap Monitor®, Sensor Devices) with its gas sampling port attached to a 10.0 mm endotracheal tube placed in 1 nostril. Rectal temperature was measured by a thermistor (Dinamap Compact Monitor T®, Critikon). The degree of muscle relaxation and anaesthesia quality was evaluated subjectively. Physiological data were collected initially when the animal first arrived at the monitoring site and then at

5 min intervals for 20 min. The roan antelope were weighed before reversal of the anaesthetics.

The animals were carried to a truck for transport and anaesthesia was reversed using i.m. or i.v. injections of naltrexone hydrochloride (NAL) (Trexonil®, 50mg/mℓ, Wildlife Pharmaceuticals, Karino) at 30 times A3080 dose and atipamezole hydrochloride (ATI) (Antisedan®, 5.0 mg/mℓ, Orion Corp., Orion-Farmos) at 3 times MED dose. The time interval from injection of reversal agents to standing and the completeness of the reversal were recorded. Animals were observed for signs of reversion to narcotisation or sedation during several hours of transport.

RESULTS

The weight range for the study group of roan antelope was 90–275 kg ($\bar{x}$ = 187 ± 68 kg). A wide range of A3080, MED and KET doses was used in this study. A3080 doses ranged from 10 to 30 µg/kg ($\bar{x}$ = 20 ± 8 µg/kg), dose ranges of MED were 5–21 µg/kg ($\bar{x}$ = 13 ± 7 µg/kg) and of KET 0.29–1.11 mg/kg ($\bar{x}$ = 0.71 ± 0.24 mg/kg). Retrospective data analysis showed that the roan antelope study group could easily be divided into a high-dose group (n = 12) and a low-dose group (n = 8). Doses for the high-dose group were A3080 (26 ± 3 µg/kg):MED (18 ± 3 µg/kg):KET (0.87 ± 0.14 mg/kg) and for the low-dose group were A3080 (11 ± 1 µ/kg):MED (5 ± 1 µg/kg):KET (0.46 ± 0.10 mg/kg).

The time to first signs of anaesthesia for the entire study group was uniformly rapid ($\bar{x}$ = 1:23 ± 0:18 min:sec SD), as was the time to recumbency ($\bar{x}$ = 2:25 ± 0:20). Comparison of time to first signs (P = 0.086) and time to recumbency (P = 0.569) between the high-dose and low-dose groups was statistically insignificant by Student's t-test. All of the inductions were reported to be similar, with each animal quickly developing variable degrees of progressive ataxia that rapidly proceeded to sternal recumbency.

The lag time from recumbency to when physiological monitoring began (time 0) had a wide range of 4:00 to 55:40 ($\bar{x}$ = 19:20 ± 14:29). The wide discrepancy in lag times between animals creates a problem of standardisation of time points during physiological monitoring and makes direct comparison of physiological variables between individual animals and animal groups problematic; however, the physiological data collected during this study provide valuable information about the physiological state and stability of the study group during the anaesthetic period.

The physiological data show uniform

stability over the designated monitoring period regardless of the disparity in the overall temporal location of physiological data points. Figure 1 shows the uniformity of the measured physiological parameters of heart and respiration rate, indirect arterial blood pressure, $ETCO_2$ and SpO_2. Mild to moderate hypoxaemia, mild hypoventilation and moderate arterial hypertension were evident throughout the monitoring period. Rectal temperature at time 0 ranged from 38.4 to 40.3 °C (39.4 ± 0.5 °C) and at the end of the monitoring period ranged from 38.0 to 40.3 °C (39.5 ± 0.6 ° C). There was no statistical difference between initial and final rectal temperatures (t-test, P = 0.598).

All animals were considered to be at an adequate plane of anaesthesia for transport, examination and for minor clinical procedures such as venipuncture throughout the monitoring period. All animals were safe for assistants to handle, did not struggle or fight, and were subjectively rated as having good generalised muscle relaxation. No regurgitation or other life-threatening phenomena occurred during the study. The length of individual anaesthetic procedures ranged from 49 to 103 min ($\bar{x}$ = 64 ± 19 min).

Anaesthesia was rapidly and completely reversed in all animals by i.m. or i.v. injections of NAL at 30 times the A3080 dose, 0.29–0.89 mg/kg ($\bar{x}$ = 0.60 ± 0.25 mg/kg), and ATI at 3 times the MED dose, 14–64 µg/kg ($\bar{x}$ = 38 ± 20 µg/kg). Time from administration of antagonists until animals were standing ranged from 3 to 16 min ($\bar{x}$ = 8 ± 4 min). No signs of relapse into narcotisation or sedation were observed during several hours of transport.

DISCUSSION

An essential characteristic of a field anaesthetic technique is a rapid, smooth, predictable induction[9] to prevent long-range movement and potential animal loss and to reduce capture-associated hyperthermia, stress, myopathy and injury. This is especially true for non-domestic ungulate species in which chemical immobilisation is considered a difficult or high-risk procedure. The combination of A3080, MED and KET, at the doses described, consistently produced very rapid onset (<2 min) and induction (<3 min) of anaesthesia in boma-confined roan antelope. The induction was also highly predictable, with animals showing variable degrees of ataxia that progressed rapidly to sternal recumbency. The early onset of anaesthetic signs together with the anxiolytic qualities of medetomidine is valuable in preventing injury and

stress-related sequelae during chemical capture.

Chemical capture of non-domestic ungulates with potent opiates alone, such as A3080, is often characterised by poor muscle relaxation with consequent hyperthermia, muscle fasciculations or trembling and compromised ventilation[3,8]. Roan antelope given potent opiates frequently have poor muscle relaxation, vocalise and, despite being unable to stand, are still able to fight handlers with their horns (SC, pers. obs., 2000). Medetomidine is known to produce good muscle relaxation in other species[4,6] and, when combined with A3080 and KET in this study, induced good generalised muscle relaxation and provided safe handling conditions.

At the dose range used in this study, the combination of A3080, MED and KET exhibited no dose-dependent effects on induction times or subjective assessment of anaesthesia quality in roan antelope. Consequently, the lower spectrum of doses (10–13 µg/kg A3080, 5–6 µg/kg MED, 0.3–0.6 mg/kg KET) is recommended for use in roan antelope. The 3-4-fold range of doses used in this study, with acceptable results, minimal effect on physiological variables and no mortality, is an indication that this drug combination has a wide margin of safety and is desirable for field capture in roan antelope.

The lag time from when animals became recumbent to when physiological monitoring began varied greatly between animals owing to procedural problems with separation of animals in the boma. The resulting temporal variation of monitoring periods within anaesthetic periods prevented statistical comparison of physiological data. However, Fig. 1 illustrates that heart rate, respiratory rate, SpO_2, $ETCO_2$ and arterial blood pressure remained relatively constant over the 20-min monitoring period. Animals experienced mild to moderate hypoxaemia as suggested by depressed oxyhaemoglobin saturation values and mild hypoventilation as suggested by elevated $ETCO_2$ values. Moderate arterial hypertension is also evident over the monitoring period as suggested by elevated indirect blood pressure values. Mild to moderate hypoxaemia, hypoventilation and hypertension should be anticipated with the use of this anaesthetic combination, since both A3080 and MED are reported to cause respiratory depression and hypertension[6,8]. Alterations in physiological values were not considered clinically significant and/ or life-threatening in this study.

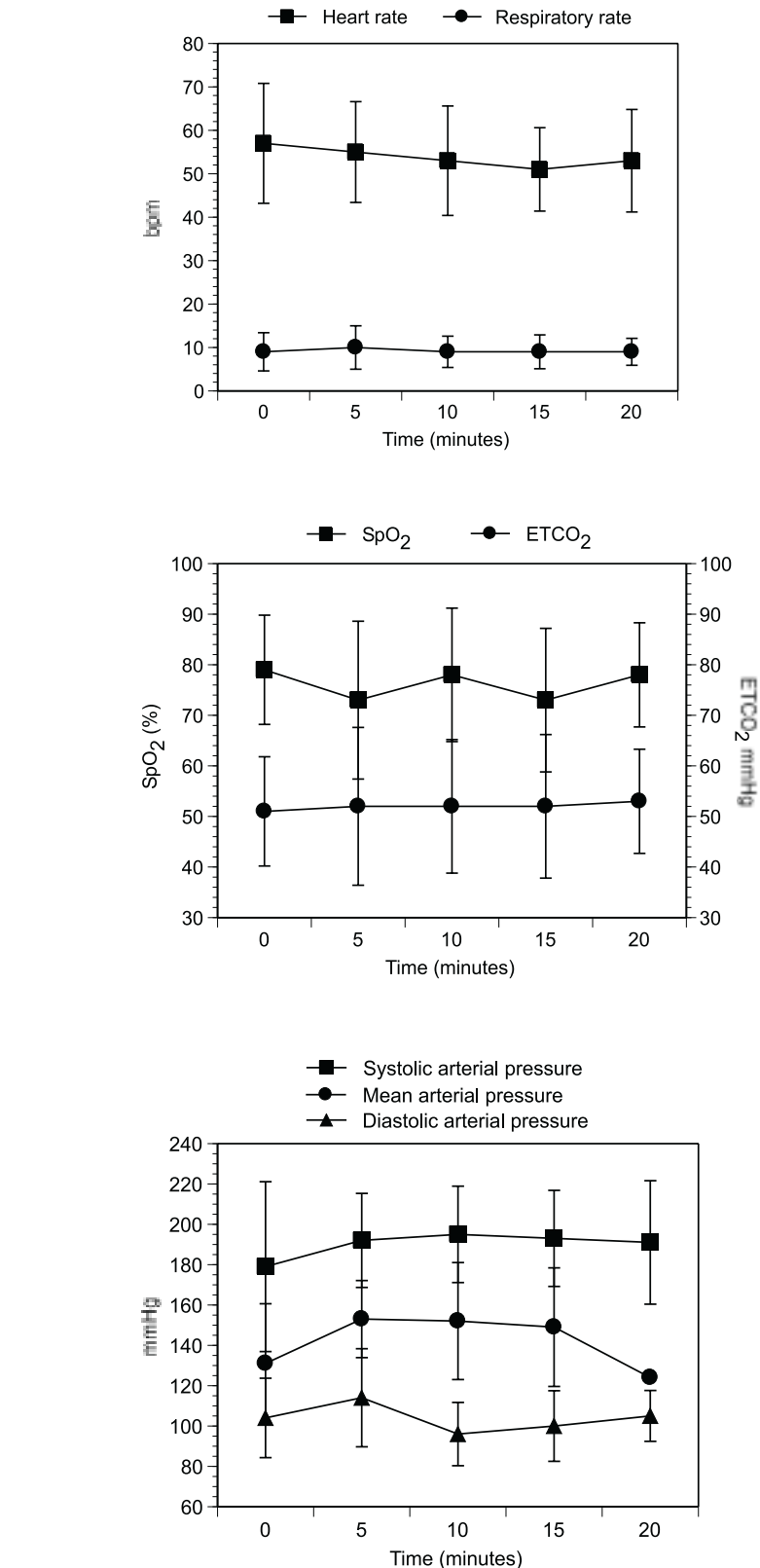Some of the key characteristics of the 'ideal' injectable drug or drug combina-

tion for chemical capture of wildlife include high therapeutic index, potency, rapid onset and induction, minimum excitement phase, good muscle relaxation, minimal cardiorespiratory depression, reversibility and rapid, smooth emergence from anaesthesia with minimal side-effects[9]. Apart from the mild to

Fig. 1: **Roan antelope physiological data collected during anaesthesia with A3080, medetomidine and ketamine during a 20-min monitoring period** (*n* = 20)**.**

moderate respiratory depression observed in this study, the combination of A3080, MED and KET appears to satisfy these criteria.

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