

Anaesthesia of nyala (*Tragelaphus angasi*) with a combination of thiafentanil (A3080), medetomidine and ketamine

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ABSTRACT

A combination of thiafentanil (A3080), medetomidine hydrochloride (MED) and ketamine hydrochloride (KET) was evaluated in 19 boma-habituated (12 female and 7 males) and 9 free-ranging nyala (7 male and 2 females) (*Tragelaphus angasi*) to develop a safe and reliable anaesthesia protocol. Wide dosages were used safely during this study with ranges for A3080 of $45 \pm 8 \mu\text{g/kg}$ with MED of $69 \pm 19 \mu\text{g/kg}$ and KET of $3.7 \pm 1.0 \text{ mg/kg}$ (200 mg/animal). The dosages developed on boma-habituated nyala proved to be equally effective in 9 adult free-ranging nyala (7 males and 2 females). The optimum dosage for nyala was a combination of A3080 ($40\text{--}50 \mu\text{g/kg}$), MED ($60\text{--}80 \mu\text{g/kg}$) plus 200 mg of KET/animal. The anaesthesia was characterised by a short induction, good muscle relaxation and mild hypoxaemia during monitoring the anaesthesia was rapidly and completely reversed by naltrexone hydrochloride (30 mg/mg of A3080) and atipamezole hydrochloride (5 mg/mg of MED) given intramuscularly. There was no mortality or morbidity associated with this protocol.

Key words: A3080, anaesthesia, atipamezole hydrochloride, ketamine hydrochloride, medetomidine hydrochloride, naltrexone hydrochloride, nyala, thiafentanil, *Tragelaphus angasi*.

Cooper D V, Grobler D, Bush M, Jessup D, Lance W **Anaesthesia of nyala (*Tragelaphus angasi*) with a combination of thiafentanil (A3080), medetomidine and ketamine.** *Journal of the South African Veterinary Association* (2005) 76(1): 18–21 (En.). Conservation and Research Center, Smithsonian National Zoological Park, 1500 Remount Road, Front Royal Virginia, VA 22630, USA.

INTRODUCTION

Nyala (*Tragelaphus angasi*) are popular and economically important species stocked on many South African game farms and a flagship species in selected national parks. They prefer a habitat of dense bush, which leads to complications when field anaesthetic protocols with long induction times are used. Nyala are fairly delicate antelope with thin skin and are predisposed to stress and capture myopathy^{6,7,14}. Traditionally, nyala are captured by a net method^{12,7} and given a tranquiliser as rapidly as possible to prevent stress and myopathy^{6,7}. There is a need to develop a rapid and safe field anaesthesia protocol for nyala applicable for remote delivery of drugs, which would

allow for individual selection of animals (e.g. trophy bulls). Reliable anaesthesia of nyala has been difficult as shown by previous reports that nyala are difficult to reliably anaesthetise and exhibit high levels of stress-related morbidity and mortality⁹ (DVC and DG, pers. obs., 2004).

Thiafentanil (A3080) is a synthetic fentanyl derivative with a rapid, pronounced opioid agonist activity. It has a shorter duration of action than carfentanil citrate (carfentanil) or etorphine hydrochloride (M99) and is only slightly less potent than carfentanil^{12,15,17,18}. A3080 given at doses approximately 3.75 and 7.5 times greater than carfentanil produced more rapid immobilisation in elk¹⁵. A3080 has a shorter induction time than carfentanil by 26–65 % in cervids¹⁶. In impala¹³ and elk¹⁸ the induction time of A3080 was dose dependent. Naltrexone hydrochloride (naltrexone) produces rapid and complete reversal of A3080 with no re-narcotisation^{13,17,18}.

Medetomidine hydrochloride (MED) is an imidazole-based compound with potent selective and highly specific agonistic activity at both pre and post-synaptic α^2 adrenoreceptors^{19,20}. It has an α^2

receptor binding affinity of 10 times that of the sedative xylazine^{11,20}. Medetomidine is a potent sedative and analgesic with anxiolytic properties^{11,19} and at high doses has hypnotic or anaesthetic effects¹⁹. Medetomidine provides good muscle relaxation with minor physiological changes in Arabian oryx (*Oryx leucoryx*)⁸ and when combined with ketamine hydrochloride (KET) has been demonstrated to be effective in a broad range of non-domestic hoofstock¹¹. A combination of KET and MED provided chemical immobilisation of impala (*Aepyceros melampus*)³ and MED combined with M99 provided adequate immobilisation of Arabian oryx for at least 3 h¹. KET has a synergistic effect when combined with MED^{3,11} and is observed to potentiate the sedative effect of synthetic opioids¹⁶.

A potent and selective α^2 adrenoreceptor antagonist, atipamezole hydrochloride (atipamezole) is highly effective in reversing sedation/anaesthesia induced by MED or MED/KET combinations in some species^{11,19}, but other species such as impala show re-sedation from MED following atipamezole³.

A pilot study was conducted on 5 boma-confined nyala (4 females and 1 male) weighing $48 \pm 7 \text{ kg}$ (average \pm SD) using a combination of A3080 ($44 \pm 14 \mu\text{g/kg}$) and 200 mg of ketamine hydrochloride (KET)/animal ($4.3 \pm 0.6 \text{ mg/kg}$). This combination resulted in initial signs in 1:15 (min:sec) with recumbency in 4 of 5 animals at 3:36 \pm 2:18 min. The nyala receiving the lowest dose of A3080 ($24 \mu\text{g/kg}$) did not become recumbent, but was easily caught. The induction time did not decrease as the dose of A3080 increased. The quality of anaesthesia was judged to be poor due to excessive struggling with difficulty of restraint, which limited collection of physiological data. The animals had elevated respiration ($31 \pm 8/\text{min}$), tachycardia ($245 \pm 22/\text{min}$) and elevated rectal temperature ($39.6 \pm 0.5^\circ\text{C}$) with good haemoglobin oxygen saturation ($91 \pm 5 \%$). Owing to poor quality of the anaesthesia and the concern for the welfare of the animal, naltrexone (30 mg/mg of A3080) was given intramuscularly (i.m.) to end the procedure within

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Received: August 2004. Accepted: November 2004.

10 min of induction. The animals stood in $1:15 \pm 0:21$ min and rapidly returned towards normal.

The objective of this study was to determine if the rapid induction attribute of A3080 could be combined with the potent selective α^2 effects of MED plus the synergism of KET with opioids¹⁶ and MED to produce a rapid-acting, balanced combination applicable to remote drug delivery in this species' dense habitat. The anaesthesia should be rapidly and completely reversible. Previous reports of this combination have been successful in producing rapid, safe and completely reversible anaesthesia in Lichtenstein's hartebeest (*Sigmoceros lichtensteinii*)⁵, roan antelope (*Hippotragus equines*)⁴ and gemsbok (*Oryx gazelle*)¹⁰.

MATERIALS AND METHODS

The study was conducted with boma-habituated and free-ranging nyala. The Kwa-Zulu Natal Nature Conservation Service captured the animals using physical methods routine in the management of this species in the Hluhluwe Umfolozi Park. The animals included both sub-adult and adult males and females that were conditioned to the bomas for at least 3 weeks prior to the study. The diet consisted of lucerne hay and commercial antelope cubes and freshly cut browse. Water was available *ad-libitum*. To mimic field conditions, food and water was not withheld prior to the anaesthesia. Their body condition and pelage was rated good by local biologists.

The bomas were approximately 5×4 m with walls constructed with closely spaced 4×13 cm wide wooden boards. A solid roof (2 m in height) covered the boma. The floors were rough-finished concrete covered with a layer of river sand. The study group consisted of 7 males and 12 females housed in bomas and 9 free-ranging adults (2 females and 7 males).

Anaesthetics were A3080 (A3080, Wildlife Pharmaceuticals, White River, South Africa), 10 mg/ml, MED (Medetomidine, Wildlife Pharmaceuticals, White River), 20 mg/ml and KET (Ketamine 200, Wildlife Pharmaceuticals, White River), 200 mg/ml. These were all formulated as sterile injectable solutions in multidose vials. The delivery system was a CO₂-powered remote injection device delivering a 3 ml air-pressurised plastic dart with a 40 mm collared needle (Dan-Inject, South Africa) to insure a deep i.m. injection.

Group 1 consisted of 19 boma-confined male and females weighing 62 ± 25 kg that received A3080 (45 ± 8 µg/kg), MED (69 ± 19 µg/kg) plus KET (200 mg/animal [3.7 ± 1.0 mg/kg]).

Table 1: Mean \pm SD dosage rates and response times in nyala anaesthetised with A3080/MED/KETM.

	Group 1	Group 2
<i>n</i>	19	9
Weight (kg)	62 ± 25	106 ± 26
A3080 (µg/kg)	45 ± 8	43 ± 3
MED (µg/kg)	69 ± 19	63 ± 9
KET (µg/kg)	3.7 ± 1.0	2.0 ± 0.7
Initial signs (min)	$1:22 \pm 0:21$	$1:48 \pm 0:18$
Recumbency (min)	$3:11 \pm 1:09$	$4:28 \pm 1:48$
NAL (mg/kg)	1.8 ± 0.7	1.3 ± 0.1
ATP (µg/kg)	340 ± 100	310 ± 50
Up (min)	$2:28 \pm 0:42$	**

**These nyala were given tranquilisers and crated; therefore the 'Up time' was compromised.

Group 2 consisted of free-ranging animals darted from a vehicle at a range of 25–40 m. The 5 adult (trophy) males (approximately 120 kg) received A3080 (5 mg) plus MED (7 mg) and 200 mg of KET/animal. The 2 adult female (approximately 60 kg) received A3080 (2.5 or 3 mg), MED (4.5 or 5 mg), respectively, plus 200 mg of KET/animal. Following monitoring these animals were placed in crates and transported to holding bomas.

Data collected included the interval from injection to 1st signs of drug effect and the time the animal became recumbent. In Group 1 initial physiological data collection (Initial Time) began in the boma after the animal became recumbent ($2:30 \pm 0:50$ min) and could be approached and safely handled. The 'Time 0' was after the animal was removed from the boma, weighed and placed in sternal recumbency at a central location for data collection ($5:45 \pm 1:25$ min). The data collection for animals in Group 2 began once the animal was moved to the site of the transport crate ($n = 2$) (Time 0). This was 3:30 and 1:20 min, respectively, after the animal was down and stable. In the other 7 nyala basic monitoring started once the animal was down and stable (lapse time was $1:40 \pm 0:50$ min).

In Group 1 the physiological parameters [heart rate, respiration rate, pulse oximetry (Nellcor N 200, Nellcor Incorp., Hayward, CA 94588, USA), and rectal temperature] and the animals' responses and muscle relaxation were evaluated and recorded. The data collected in Group 2 included initial signs, down time, heart rate, respiration rate, rectal temperature and muscle relaxation. Pulse oximetry readings were limited to 2 animals, a complete 15 min monitoring in 1 male and a 15 min reading in a 2nd male.

The A3080 was reversed using i.m. naltrexone (Trexonil®, naltrexone HCl, Wildlife Laboratories, Fort Collins, CO) at a dosage of 30 mg/mg of A3080. The MED was reversed using i.m. atipamezole (Antisedan®, atipamezole HCl, Pfizer

Animal Health, Exton, PA) at a dosage of 5 mg/mg of MED. The time to standing and completeness of recovery were recorded. The anaesthetised free-ranging nyala were crated and given tranquilisers [150 mg perphenazine enanthate (Trilifon Enanthate, Schering-Plough, Isando, South Africa) i.m. plus 15 mg haloperidol (Haloperidol®, Kyron Laboratories, Johannesburg) intravenously (i.v.)] at the time of the naltrexone and atipamezole injections. This is the standard protocol of the Natal Parks Board Game Capture Unit when placing field captured nyala into a boma, therefore the full extent of recovery from the naltrexone and atipamezole could not be evaluated completely in this group.

RESULTS

Group 1 received a combination of A3080, MED and KET and showed signs at $1:22 \pm 0:21$ min with recumbency at $3:11 \pm 1:09$ min (Table 1). Neither the onset or down time was related to the dosage of A3080 or MED. The quality of the anaesthesia was good to excellent depending on the degree of muscle relaxation and ease of handling. The improved quality of the anaesthesia and muscle relaxation was correlated to the increasing dosage of MED rather than an increasing dose of A3080.

The physiological data from Group 1 (Table 2) shows acceptable heart and respiration rates with the higher rates for both recorded initially when the animal became recumbent and in animals receiving the lower dosages of either A3080 or MED. The average haemoglobin oxygen saturation ranged from 80 to 86 %, with the lower values seen at initial recumbency, while 15 min later the value improved. The average initial rectal temperature was 39.6 °C and only rose to 39.8 °C by the end of the monitoring period. An area of piloerection of 4–8 cm was noted in 12 animals around the dart site prior to recumbency. Eight females and 2 males exhibited pelvic thrusting prior to recum-

Table 2: Physiological data of nyala anaesthetised with A3080/MED/KET including respiration rate, heart rate, oxygen saturation and body temperature. Mean \pm SD.

	Group 1	Group 2
<i>n</i>	19	9
Respiration rate		
Initial	24 \pm 10	
0 time	14 \pm 6	24 \pm 5
5 min	15 \pm 7	16 \pm 8
10 min	13 \pm 5	19 \pm 1
15 min	15 \pm 4	18 \pm 2
Heart rate		
Initial	144 \pm 46	
0 time	106 \pm 45	81 \pm 11
5 min	95 \pm 32	68 \pm 5
10 min	91 \pm 15	67 \pm 10
15 min	90 \pm 13	69 \pm 3
O₂ saturation		
5 min	80 \pm 16	72*
10 min	82 \pm 11	80*
15 min	86 \pm 8	86**
Temperature (C)		
Initial	39.6 \pm 0.5	39.1 \pm 0.46
End	39.8 \pm 0.7	39.3 \pm 0.52

**Only 1 reading was obtained on 1 animal for this period.

*Average of readings on 2 animals for this period.

bency. The quality of the anaesthesia was good in all but one male receiving a lower than average dosage of both A3080 (37 μ g/kg) and MED (55 μ g/kg).

The Group 2 free-ranging nyala were darted by vehicle at ranges of up to 40 m. Five of the 9 animals showed 1st signs at 1:48 \pm 0:18 min with recumbency at 4:28 \pm 1:48 min. The other 4 briefly disappeared into the dense bush, which precluded obtaining initial signs and time of recumbency, but all were found recumbent in an average of 11 min. The estimated distance travelled by all Group 2 nyala after darting was less than 40 m. Pelvic thrusting was observed in both females.

Data from Group 2 was comparable to the boma-confined nyala with the exception of slower heart rates (Table 2). Two male nyala had more complete physiological data sets, and 7 only heart rate, respiration and body temperature collected twice. The anaesthesia was good in all animals with good muscle relaxation, which facilitated handling and crating.

The recoveries of the nyala in both groups were comparable. Following the i.m. injection of naltrexone and atipamezole the average time to standing in Group 1 was 2:28 \pm 0:42 min. The recovery progressed rapidly with the animals appearing to be 90 % recovered within 8–10 min. The recovery was smooth with the animal first gaining control of its head and maintaining a sternal position until standing in a controlled manner. Most nyala regained their feet on the 1st attempt. The exceptions were the field-anaesthetised nyala in Group 2, which received i.v. and i.m.

tranquilisers and placed in crates. Their recovery was rapid to the point where they were sternal with control of their heads within 2–4 min, but they remained quiet in the crate and eventually stood in 10–20 min, which is desirable for crated animals.

DISCUSSION

Ketamine at 200 mg/animal was a constant throughout this study. This dosage was selected since this volume filled the 3 ml dart and was beneficial in previous studies^{4,5,10}.

Ketamine has synergistic properties with both MED^{3,11} and opiates¹⁶ which decrease the dosages of MED and A3080 and gains the dissociative properties of KET to assist in the rapid down time. This dosage of KET was not observed to cause a residual problem following the reversal of A3080 and MED.

In the pilot study using only A3080 and KET, there was a rapid onset and down time, but the quality of the anaesthesia was poor due to the muscle rigidity and excessive struggling. To decrease the rigidity induced by the opiate, A3080, a powerful rapid-acting α^2 agonist (MED) was added to Groups 1 and 2. This combination also produced a rapid onset and recumbency, plus having an animal that was relaxed and manageable. The addition of MED resulted in a lower haemoglobin oxygen saturation, but the benefits of the relaxation outweighed the decreased haemoglobin oxygen saturation. With the A3080/MED/KET combination it was observed that nyala were oblivious to their surroundings within

1:30 min of darting making physical capture easy; in addition the distance travelled after darting was short with appropriate dosages, which proved to be an advantage in the Group 2 free-ranging animals.

The physiological parameters measured during this study were maintained within an acceptable range with the exception of initial hypoxia, which improved over the monitoring period. All animals exhibited an initial increased respiration and heart rate, which over the next 15 min slowed to an acceptable rate.

The piloerection at the dart site was seen in 12 animals and was attributed to MED as reported in impala³. The piloerection is useful in a field situation to help follow the animal if the dart falls out. The cause of the pelvic thrusting is not fully understood, but surprisingly was observed more commonly in females (10 of 14) compared with males (2 of 14).

The antagonists (naltrexone and atipamezole) were given i.m. and resulted in a controlled, rapid and complete reversal. When these drugs were given i.v. in other species the reversal was very rapid and the animals had a tendency to stumble or crash into fixed objects³.

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