RESEARCH PAPER

Butorphanol–azaperone–medetomidine and ketamine–butorphanol–azaperone–medetomidine chemical immobilization in habituated subadult female giraffe (*Giraffa camelopardalis*)

Silke Pfitzer[a], Liesel L Laubscher[b], Jacobus P Raath[b], Aleksandr Semjonov[c], Etienne P Basson[d,e], Lisa L Wolfe[f], Michael W Miller[f] & Gareth E Zeiler[d,e]

[a]Department of Nature Conservation, Tshwane University of Technology, Pretoria, South Africa

[b]Wildlife Pharmaceuticals Pty (Ltd.), Mpumalanga, South Africa

[c]The Institute of Veterinary Medicine and Animal Sciences, Estonian University of Life Sciences, Tartu, Estonia

[d]Department of Companion Animal Clinical Studies, Faculty of Veterinary Science, University of Pretoria, Onderstepoort, South Africa

[e]Section of Anaesthesiology & Critical Care Services, Valley Farm Animal Hospital, Pretoria, South Africa

[f]Colorado Division of Parks and Wildlife, Fort Collins, CO, USA

Correspondence: Silke Pfitzer, Department of Nature Conservation, Tshwane University of Technology, Private Bag X680, Pretoria 0001, South Africa. E-mail: Pfitzers@tut.ac.za

Abstract

Objective To describe the effects of butorphanol–azaperone–medetomidine (BAM) and ketamine–butorphanol–azaperone–medetomidine (KBAM) used for the chemical immobilization of giraffes.

Study design Quasi-experimental trial.

Animals A group of 10 habituated subadult female giraffes.

Methods Five giraffe were immobilized with BAM (0.02 mL cm^{-1} estimated shoulder height) and five with KBAM (0.015 mL cm^{-1} estimated shoulder height BAM and 200 mg ketamine). Time to events were recorded (time to recumbency and recovery time). Physiological variables (heart rate, respiratory rate, rectal temperature, invasive arterial blood pressure and peripheral oxyhaemoglobin saturation) were recorded every 5 minutes and arterial blood gas analysis was performed every 10 minutes after instrumentation. Atipamezole (5 mg mg^{-1} medetomidine administered) and naltrexone (1 mg mg^{-1} butorphanol administered) were administered intramuscularly at 30 minutes post-recumbency for recovery. Time to events, physiological and arterial blood gas data were compared between drug combinations using a two-sample *t*-test (significance was $p < 0.05$). Data are shown as mean ± standard deviations.

Results All giraffes were successfully immobilized. Based on measured shoulder height, the doses administered were 0.70 and 0.48 mg cm^{-1} for butorphanol, 0.28 and 0.2 mg cm^{-1} for azaperone and medetomidine in BAM and KBAM, respectively. Times to recumbency were 17.1 ± 9.3 and 6.3 ± 1.1 minutes for BAM and KBAM respectively ($p = 0.06$). All giraffes had hypoxaemia and hyperlactataemia, with PaO_2 values of 52 ± 13 and 41 ± 4 mmHg and lactate values of 14.4 ± 6.1 and 11.0 ± 5.5 mmol L^{-1} for BAM and KBAM, respectively. Recoveries were calm with minimal ataxia.

Conclusion and clinical relevance BAM and KBAM produced reliable chemical immobilization for 30 minutes. The addition of ketamine to the BAM combination is recommended because of its faster induction time. Because of clinically significant hypoxaemia, oxygen supplementation should be administered if these drug combinations are used.

Keywords BAM, giraffe, immobilization, KBAM.

Introduction

Giraffe (*Giraffa camelopardalis*) are ungulates that belong to the family *Giraffidae* in the order Ruminantia (Apps 2000). Nine subspecies of giraffe are currently recognized, and they are commonly kept in zoological collections all over the world

(Dagg 2014). With an estimated 68,000 animals left in the wild, giraffes are classified by the International Union for the Conservation of Nature (IUCN) as vulnerable (O'Connor et al. 2019).

Although immobilization of this species is becoming more common owing to conservation efforts and the need for husbandry care in captive sanctuaries and zoo collections, the chemical immobilization of giraffes continues to be a highly challenging process. Owing to their size, unusual anatomy and physiology, immobilization is associated with risk of harm to both the animal and personnel (Vogelnest & Ralph 1997; Bush et al. 2001, 2002). Potent opioids such as etorphine, carfentanil and thiafentanil alone or in combination with sedatives have been used for decades to immobilize free-ranging and captive giraffes (Langman 1973; York et al. 1973; Bush et al. 1976; Bush & Vos 1987). However, potent opioids are not readily available worldwide because of regulatory constraints. Therefore, alternative drug combinations that use readily available non-potent opioid drugs, such as butorphanol, medetomidine, azaperone and ketamine, been investigated alone or in various combinations in a wide range of free-ranging and captive ungulates (Mich et al. 2008; Miller et al. 2009; Chittick et al. 2012; Wolfe et al. 2014; Lapid & Shilo-Benjamini 2015; Hansen & Beckmen 2018; Harms et al. 2018; Semjonov et al. 2018).

A premixed combination of butorphanol—azaperone—medetomidine (BAM) has been investigated for chemical immobilization in Thomson's gazelles (*Gazella thomsoni*) (Chittick et al. 2012), caribou (*Rangifer tarandus granti*) (Hansen & Beckmen 2018), bison (*Bison bison*) (Harms et al. 2018), Nubian ibex (*Capra nubiana*) (Lapid & Shilo-Benjamini 2015), white-tailed deer (*Odocoileus virginianus*) (Mich et al. 2008; Miller et al. 2009), blesbok (*Damaliscus pygargus phillipsi*) (Semjonov et al. 2018), sable antelope (Dittmer et al. 2023) and Rocky Mountain elk (*Cervus canadensis nelsoni*) (Wolfe et al. 2014). The BAM combination reliably provided immobilization in these species, especially if the animals were habituated to captivity. Wildlife veterinarians experienced in free-ranging ungulate chemical immobilization recommend the addition of ketamine to the BAM drug combination (KBAM) to improve the reliability of the induction and immobilization (Kreeger et al. 2023). This recommendation likely arose from many studies where ketamine-α_2-adrenoceptor agonist combinations have been successfully used in ungulate immobilization, including free-ranging and captive giraffe (Bush et al. 2001, 2002; Lamberski et al. 2004; Delk et al. 2019).

The aim of this study was to assess the practicality of using BAM and KBAM for the chemical immobilization of giraffes, and to describe and compare their effects, where possible. We hypothesized that both drug combinations, when administered intramuscularly via projectile dart, would reliably and effectively induce a recumbent state of chemical immobilization without causing clinically significant cardiopulmonary physiological derangements in immobilized giraffes.

Materials and methods

Study design, treatments and animals

Animal ethics approval was obtained before the commencement of this trial (WPAEC-2017-BAMGIR-12-B). This study was reported using the ARRIVE guidelines 2.0. A quasi-experimental trial was conducted using opportunistic data collection. Owing to the opportunistic nature of the study, a sample size calculation was not performed. A group of 10 subadult female free-ranging giraffes (aged between 3 and 4 years) were captured and transported to a wildlife holding facility (Trados Game Farm, RSA). At the facility, after a 2 week habituation period, the giraffes underwent chemical immobilization for routine health examination and bloodwork before being translocated to another undisclosed location. Because of safety concerns associated with immobilizing giraffes, the investigators chose not to blind the study and not to randomize the administration of the two different drug combinations. The first five giraffes were immobilized with a proprietary fixed dose combination of butorphanol (30 mg mL^{-1}), azaperone (12 mg mL^{-1}) and medetomidine (12 mg mL^{-1}) (BAM) [Wildlife Pharmaceuticals South Africa (Pty) Ltd., RSA]. The remaining five giraffe were immobilized with a combination of ketamine [200 mg mL^{-1}; Wildlife Pharmaceuticals South Africa (Pty) Ltd.] and BAM. At the holding facility, the giraffes were cared for and fed [lucerne (*Medicago sativa*) hay, game pellets and fresh browsing foliage in the form of fresh cut tree branches from various tree species suspended on the walls of the pen] by experienced caretakers and veterinary staff working at the facility. Potable water was freely accessible *ab libitum*. The purpose-built giraffe rectangular pens were 8 m by 10 m in surface area and walls were 4 m high. Giraffes were housed in small groups using four pens in total. Shelter from the elements were provided by galvanized zinc roofs and tall trees within the pen. Before the commencement of the drug trials, giraffes were deemed healthy based on their bloodwork results and regular consumption of food and water, passing normal stools with no signs of weakness or depression.

Study procedures

Before commencing the study procedures, a temporary circular enclosure made of suspended plastic sheeting was constructed near the entrance of a corridor leading to the pens. The enclosure measured approximately 30 m in diameter and 3.5 m in height. There was no padding attached to the plastic walls, nor were there any devices placed to assist the giraffe during induction and recovery using ropes. The surface was

mostly sandy with sparsely located patches of grass and approximately five thin-stemmed (<100 mm diameter) trees close to the inner perimeter, typical of the veld in this geographical region. This circular enclosure was used to immobilize the giraffe one-at-a-time during the study. The shoulder height of each giraffe was estimated by an experienced wildlife veterinarian to standardize the volume (and thus dose) of drugs administered during darting. The shoulder height was estimated visually from the dorsal aspect of the shoulders (withers), perpendicular to the ground as they walked past a pole of a known height. A body mass scale large enough to accommodate giraffe was not available and therefore estimated shoulder height was used, as previously described for giraffe (Bush et al. 2001).

The planned BAM drug combination dosage was 0.02 mL cm^{-1} estimated shoulder height. In contrast, the planned ketamine dose was fixed at 200 mg per giraffe (i.e. 1 mL of ketamine) mixed with 0.015 mL cm^{-1} estimated shoulder height of BAM in the KBAM drug combination. For all immobilizations, the total volume of drugs exceeded 3 mL which was the capacity of the darts available during the study. Therefore, the total BAM drug volume was divided equally into two 3 mL darts fitted with a 50.8 mm (2 inch) long 13 gauge needle (Pneu-Dart Type 'P'; Pneu-dart Inc., PA, USA). In KBAM, the 1 mL of ketamine was divided equally between the two darts.

On the days of data collection, food and water were withheld for 12 hours before immobilization. A giraffe was randomly selected and herded into the temporary circular enclosure and left alone for 15 minutes. The darts were prepared and then after the 15 minute period, the drug-loaded darts were fired one-at-a-time from a carbon dioxide (CO_2)-powered dart projector (X-Caliber; Pneu-Dart Inc.) by an experienced wildlife veterinarian. Both darts were fired at and placed in the large muscle groups of the proximal pelvic limb within 10 seconds of each other. Once both darts were placed and confirmed to have discharged their contents, a stopwatch was then started immediately to record time to various events. The induction consisted of two phases. The first phase was waiting for visual cues of a drug effect and signs of sedation which included an open mouth with a flaccid tongue hanging out, ataxic gait and lowering of the head (recorded as time to first drug effect). The second phase consisted of the giraffe becoming sternally or laterally recumbent (recorded as time to recumbency). Once recumbent, the head and neck were placed on a wooden board (1200 mm × 450 mm × 20 mm) with their nose positioned below the level of the oropharynx. The head end of the board was elevated above the level of the rumen by resting it on top of hay bales to provide a slope of approximately 40 degrees to the ground. The giraffe was blindfolded, and cotton wool was pushed into the external ear canals with the aim of reducing external stimuli. The trachea was intubated by palpating the *rima glottidis* and advancing a cuffed silicone endotracheal tube (22−26 mm; Kruuse, Denmark) into the proximal trachea and the cuff was inflated with 50 mL of room air. A 22 gauge Jelco catheter (Midlands Veterinary Wholesalers, RSA) was aseptically placed into the auricular artery of the dependent ear. Pulse rate and invasive arterial blood pressure were measured from this catheter using a portable monitor (IntraTorr; IntraVitals, UK). Peripheral haemoglobin oxygen saturation (SpO_2) was assessed using a pulse oximeter (Nonin PalmSAT 2500; Nonin, The Netherlands) with a reflectance probe taped to the skin under the proximal ventral tail (approximately 5 cm away from the anus), as previously described in other wildlife ungulates (Mtetwa et al. 2020). Rectal temperature (RT) was measured with a digital thermometer (Pigeon 10800 soft tip; Pigeon, RSA). Cardiac auscultation using a stethoscope and manual counts of exhaled breaths (f_R) were recorded every 5 minutes. Once instrumented, continuous physiologic monitoring started (T0) and recorded at 5 minute intervals (T5, T10, T15, T20) until 25 minutes (T25). A 1 mL arterial blood sample was anaerobically collected into pre-heparinized syringes (BD-A line; Midlands Veterinary Wholesalers) and analysed using a portable blood gas analyser (i-STAT Portable Clinical Analyzer; Abaxis, CA, USA) and self-calibrating cartridges (i-STAT cartridges CG4+ and CHEM8; Abaxis) at T0, T10 and T20. During the monitoring period, the actual shoulder height was measured using a tape measure from the sole of the hoof on the stretched out nondependent thoracic limb to the dorsal aspect of the shoulder region (i.e. withers region). Throughout the procedure, the neck of the giraffe was massaged to prevent muscle spasms.

After T25, all monitoring equipment and ear plugs were removed from the enclosure, the neck board was removed and the head was placed on the ground. The giraffe's trachea was extubated and the arterial catheter removed. At 30 minutes (T30), reversal drugs were injected into the muscles of the proximal pelvic limb, as follows: atipamezole (Antisedan 5 mg mL^{-1}; Orion Pharma, Finland) was dosed at 5 mg per 1 mg of medetomidine administered; naltrexone hydrochloride (Trexonil 50 mg mL^{-1}; Wildlife Pharmaceuticals South Africa (Pty) Ltd.) was dosed at 1 mg per 1 mg of butorphanol administered. A team of three to five experienced assistants knelt alongside the dorsal aspect of the giraffe's neck while it was in lateral recumbency and manually held the head and proximal neck down. The aim was to prevent early attempts to move into sternal recumbency or stand. If the giraffe was strong enough to overpower the assistants, then the blindfold was removed, and they moved to a safe location away from the giraffe as it attempted to move into sternal recumbency or stand. The time to standing was recorded from completing the injection of antagonists until the giraffe stood. The time to full recovery was recorded from completion of the injection of antagonists until the giraffe was walking in a coordinated way and able to retain its tongue within the oral cavity. Once fully recovered,

., 52, 403−411

the giraffe was herded back to its pen. All giraffes were in good health and relocated a week after the study concluded to an undisclosed private game farm.

Data collection and analysis

Physiological data [heart rate (HR), f_R, systolic (SAP), mean (MAP) and diastolic arterial blood pressures (DAP), RT and SpO_2) were recorded on a data collection sheet. Time to first drug effect, recumbency, standing and full recovery were recorded. Data from arterial blood gas included measured pH, partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$), lactate and calculated base excess (BE) and arterial oxygen haemoglobin saturation (SaO_2). The actual BAM dose was calculated based on the measured shoulder height as follows:

Volume of BAM (mL)/shoulder height (cm) = mL/cm shoulder height

mL/cm shoulder height × mg/ml of each drug = mg of drug/cm shoulder height

Statistical analysis

Data were assessed for normality by inspecting descriptive statistics and histograms and applying the Ryan–Joiner normality test. Data were normally distributed, and results were reported as mean ± 95% confidence intervals (95% CI). Physiological data within each treatment were inspected on interval plots of the mean and 95% CI of the mean over time. There was no visual evidence of changes in value over time. Therefore, physiological data were averaged over time for each giraffe and then compared between drug combinations using a two-sample *t*-test. The same method of analysis was applied to the arterial blood gas data analysis as for physiological data. The times to events were also compared between drug combinations using a *t*-test. For all *t*-tests, the effect size was determined by calculating Cohen *d*. Agreement between paired SaO_2 and SpO_2 data (T0, T10, T20) was determined using a Bland–Altman plot where the differences of the means were plotted as a percentage (%). A maximum clinically acceptable agreement was defined as a bias of 10%. Physiological data were presented in the form of interval plots of the mean and 95% CI of the mean over time. Arterial blood gas data and times to events are presented in Tables 1 and 3. Data were assessed using commercially available software (MiniTab, version 18.1; MiniTab Inc., PA, USA) and significance was interpreted as $p < 0.05$.

Results

All giraffes were successfully chemically immobilized and relocated at the end of the study. The measured mean (95% CI) shoulder height for giraffes administered BAM and KBAM was 222 (201–243) cm and 216 (208–224) cm, respectively, ($p = 0.470$). The volume of BAM administered to giraffes in the BAM combination was 0.023 (0.018–0.029) mL cm^{-1} shoulder height, and 0.016 (0.009–0.023) mL cm^{-1} shoulder height for KBAM. Therefore, the dose of butorphanol administered was 0.70 (0.54–0.87) and 0.48 (0.28–0.69) mg cm^{-1} shoulder height for BAM and KBAM, respectively. The azaperone and medetomidine drug concentrations were the same in the premix which resulted in the same doses administered per drug combination. Azaperone and medetomidine doses were both 0.28 (0.22–0.35) mg cm^{-1} shoulder height for BAM and 0.20 (0.12–0.27) mg cm^{-1} shoulder height for KBAM. Giraffes ambulated with a progressively ataxic gait until stumbling into a recumbent state. Two giraffes in each group would, after a period of ataxic ambulation, stand and rock on their feet before dropping into a sternal recumbency and had to be blindfolded and pulled into lateral recumbency

Table 1 Comparison of means for time events in boma habituated female giraffe immobilized with butorphanol–azaperone–medetomidine (BAM; $n = 5$) and ketamine–butorphanol–azaperone–medetomidine (KBAM; $n = 5$). CI, confidence interval; Diff, difference; SD, standard deviation; SE, standard error.

Variable (minutes)	Group	Mean	±SD	SE	Diff	(95% CI for difference)	*p*-value	Cohen *d*
First drug effect	BAM	3.0	0.6	0.3	0.3	(−0.6 to 1.2)	0.46	0.50
	KBAM	2.7	0.6	0.3				
Recumbency	BAM	17.1	9.3	4.2	10.8	(−0.9 to 22.4)	0.06	1.63
	KBAM	6.3	1.1	0.5				
Onset of recovery	BAM	2.1	0.8	0.4	−0.6	(−2.0 to 0.7)	0.31	0.69
	KBAM	2.7	1.0	0.4				
Standing	BAM	6.3	1.6	0.7	−2.1	(−5.3 to 1.2)	0.17	0.98
	KBAM	8.4	2.5	1.1				
Fully recovered	BAM	6.8	1.4	0.6	−2.4	(−6.3 to 1.5)	0.17	0.69
	KBAM	9.2	3.1	1.4				

by the assistants. No major injuries or debilitating head crashes occurred in any giraffes. The mean recumbency time for BAM was 17.1 (5.5–28.6) minutes and although not significantly longer in duration, it was clinically relevant compared with 6.3 (5.0–7.6) minutes for KBAM ($p = 0.06$; Table 1).

None of the physiological variables were significantly different between BAM and KBAM (Fig. 1 & Table 2). Physiological variable values need to be interpreted in light of the fact that time to recumbency was longer in the BAM group than in the KBAM group. The HR was 55 (44–65) beats minute^{-1} for BAM and 46 (27–65) beats minute^{-1} for KBAM. The f_R was high with both combinations, 65 (62–69) breaths minute^{-1} for BAM and 65 (54–76) breaths minute^{-1} for KBAM. The RT was 39.3 (37.4–41.3) °C for BAM and 39.2 (37.8–40.7) °C for KBAM. SAP was 192 (154–229) mmHg for BAM and 183 (174–192) mmHg for KBAM. DAP was 97

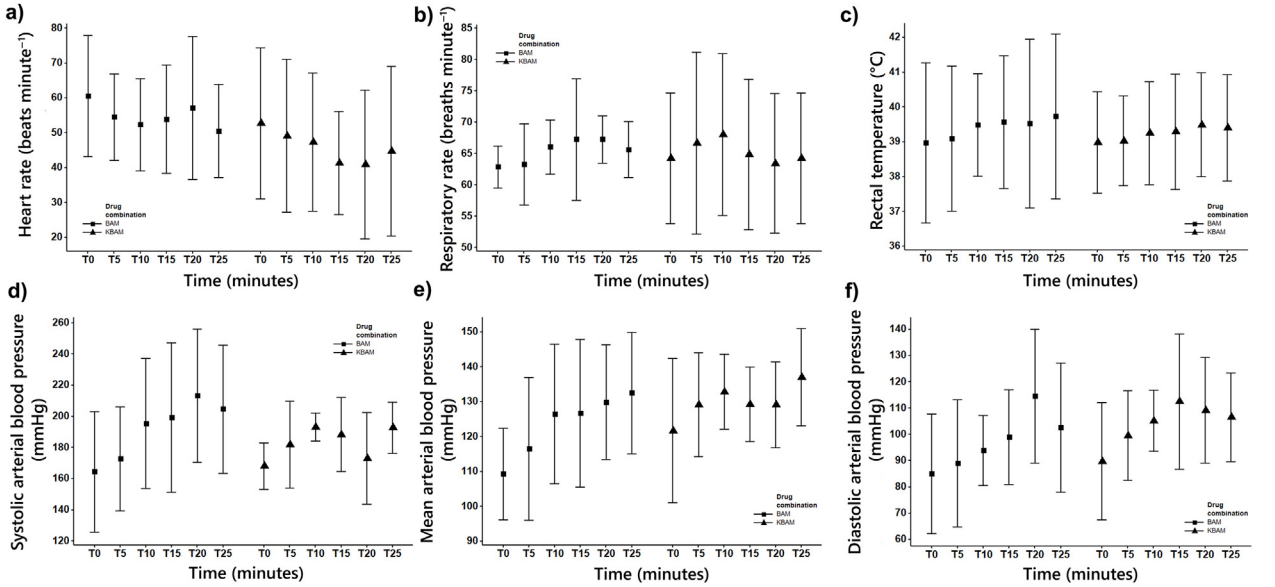

Figure 1 Mean (and 95% confidence intervals of the mean) values for heart rate (a), respiratory rate (b), rectal temperature (c) and systolic (d), mean (e) and diastolic (f) arterial blood pressure (invasive measurement) in female giraffe immobilized using butorphanol–azaperone–medetomidine (BAM; $n = 5$) and ketamine–butorphanol–azaperone–medetomidine (KBAM; $n = 5$).

Table 2 Comparison of averaged means (over six time points) for physiological data in boma habituated female giraffe immobilized with butorphanol–azaperone–medetomidine (BAM; $n = 5$) and ketamine–butorphanol–azaperone–medetomidine (KBAM; $n = 5$). CI, confidence interval; DAP, diastolic arterial pressure; Diff, difference; f_R, respiratory rate; HR, heart rate; MAP, mean arterial pressure; SAP, systolic arterial pressure; SD, standard deviation; SE, standard error; SpO_2, haemoglobin saturation with oxygen; Temp, temperature.

Variable	Group	Unit	Mean	±SD	SE	Diff	(95% CI for difference)	*p*-value	Cohen *d*
HR	BAM	beats minute^{-1}	55	8	4	8.8	(−10.2 to 27.8)	0.30	0.72
	KBAM		46	15	7				
f_R	BAM	breaths minute^{-1}	65	3	1	0.1	(−11.3 to 11.5)	0.98	0.00
	KBAM		65	9	4				
SpO_2	BAM	%	97	2	1	1.8	(−1.5 to 5.0)	0.24	0.88
	KBAM		95	2	1				
Temp	BAM	°C	39.3	1.6	0.7	0.1	(−2.0 to 2.2)	0.92	0.04
	KBAM		39.2	1.2	0.5				
SAP	BAM	mmHg	192	30	13	8.9	(−29.4 to 47.2)	0.56	0.40
	KBAM		183	7	3				
DAP	BAM	mmHg	97	12	5	−6.7	(−23.7 to 10.2)	0.38	0.56
	KBAM		104	11	5				
MAP	BAM	mmHg	125	14	6	−5.3	(−23.8 to 13.3)	0.51	0.44
	KBAM		130	9	4				

(82–112) mmHg for BAM and 104 (90–117) mmHg for KBAM. MAP was 125 (107–142) mmHg for BAM and 130 (119–141) mmHg for KBAM. There was poor agreement between SaO_2 and SpO_2 and almost all data points exceeded the maximum clinically acceptable bias of 10% (Fig. 2). For arterial blood gas analysis, the pH of the arterial blood was 7.36 (7.25–7.48) for BAM and 7.27 (7.11–7.42) for KBAM (Table 3). All giraffes were hypoxaemic and had a PaO_2 of 52 (36–68) mmHg for BAM and 41 (35–46) mmHg for KBAM. Overall, BAM-immobilized giraffes were hypocapnic with a $PaCO_2$ of 33 (30–37) mmHg or normocapnic with 42 (35–49) mmHg for KBAM ($p = 0.03$). All giraffes had hyperlactataemia with a lactate concentration of 14.4 (6.9–22.0) mmol L^{-1} for BAM and 11.0 (4.2–17.9) mmol L^{-1} for KBAM.

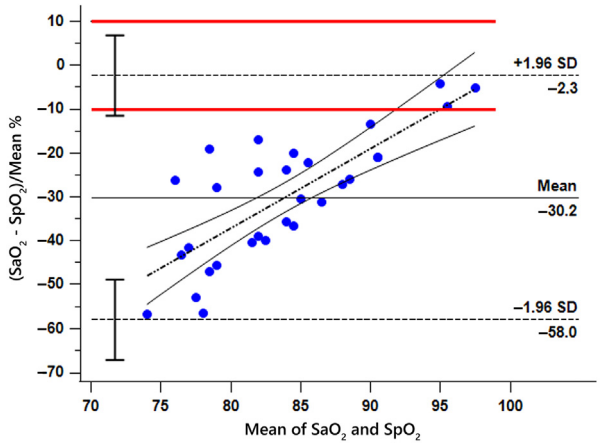

Figure 2 Bland–Altman plot of co-oximeter-measured oxyhaemoglobin saturation of arterial blood (SaO_2) *versus* pulse oximeter-measured peripheral oxyhaemoglobin saturation (SpO_2, using a reflectance probe under the tail). Acceptable limits were set to ± 10% (red lines), SD; standard deviation. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Recovery was overall calm, with the giraffes lifting their heads and moving into sternal recumbency once they were able to overpower the assistants. They waited a brief period before attempting to stand, which was often achieved in one or two well-coordinated attempts. Once standing, most giraffes walked steadily with minimal ataxia. However, two of the five giraffes immobilized with KBAM overpowered the assistants too early and their attempts to move into sternal recumbency and to stand were uncoordinated. Although appearing dramatic in their attempts to stand, no visible minor (abrasions) or major (dislocations and fractures) injuries were sustained.

Discussion

Giraffes with their distinctive anatomy, physiology and behavioural characteristics present a unique challenge when chemical immobilization is required for handling or translocation (Citino et al. 2006). The two drug combinations evaluated in this study BAM and KBAM were assessed for their efficacy for chemical immobilization in subadult female giraffes. Both drug combinations yielded stable immobilizations and uneventful recoveries, although hypoxaemia was a clinical concern. Given the unique body conformation of giraffes,

Table 3 Comparison of averaged means (over three time points) for blood gas analysis in boma habituated female giraffe immobilized with butorphanol–azaperone–medetomidine (BAM; $n = 5$) and ketamine–butorphanol–azaperone–medetomidine (KBAM; $n = 5$). BE, base excess; CI, confidence interval; Diff, difference; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SD, standard deviation; SE, standard error, SO_2, calculated oxyhaemoglobin saturation.

Variable	Group	Unit	Mean	±SD	SE	Diff	(95% CI for difference)	*p*-value	Cohen *d*
pH	BAM	–	7.36	0.09	0.04	0.10	(−0.06 to 0.26)	0.20	0.89
	KBAM		7.27	0.12	0.06				
PaO_2	BAM	mmHg	52	13	5.7	11.5	(−5.2 to 28.1)	0.13	1.22
	KBAM		41	4	1.9				
PaO_2	BAM	kPa	6.9	1.7	0.8				
	KBAM		5.5	0.5	0.3				
$PaCO_2$	BAM	mmHg	33	3	1.3	−8.6	(−16.2 to −1.00)	0.03	1.86
	KBAM		42	6	2.7				
$PaCO_2$	BAM	kPa	4.4	0.4	0.2				
	KBAM		5.6	0.8	0.4				
BE	BAM	mmol L^{-1}	−13.5	7.5	3.3	−5.9	(−16.0 to 4.3)	0.21	0.81
	KBAM		−7.6	6.0	2.7				
SaO_2	BAM	%	76	11	4.9	8.3	(−6.3 to 22.9)	0.22	0.87
	KBAM		67	8	3.7				
Lactate	BAM	mmol L^{-1}	14.4	6.1	2.7	3.4	(−5.3 to 12.1)	0.39	0.59
	KBAM		11.0	5.5	2.5				

weight estimations are often highly inaccurate, making height-based dosing a more reliable approach (Bush et al. 2001).

One of the noteworthy findings of this study was the difference in induction time between BAM and KBAM. Although not statistically significant (most likely because of small sample size), this difference was clinically meaningful. On average, giraffes immobilized with KBAM became recumbent over 10 minutes faster than those immobilized with BAM alone. In wildlife, consistent, fast inductions are crucial to reduce the risk of injury, stress and activity-induced hyperthermia. In captive giraffes, induction times with medetomidine–ketamine varied from 4 to 38 minutes (Lamberski et al. 2004; Delk et al. 2019). The addition of thiafentanil to the combination did not significantly shorten the induction time, which reportedly ranges from 3 to 26 minutes (Citino et al. 2006; Delk et al. 2019; Roeder et al. 2024). However, this combination (thiafentanil–medetomidine–ketamine) improves immobilization quality and provides increased analgesia, making it preferable for longer procedures in captive giraffes (Citino et al. 2006; Roeder et al. 2024). A study by Sailler et al. (2024) examined a two-stage darting method in which giraffes were first darted with ketamine–xylazine, followed 15–20 minutes later by thiafentanil–etorphine. This approach resulted in initial signs of sedation within 11 minutes after the first dart and recumbency within 6 minutes after the second. Compared with all these studies, the KBAM combination in the current study seems to provide a fast and consistent induction with a time to recumbency of 6.3 ± 1.1 minutes.

Both BAM and KBAM were effective in maintaining physiological stability, with no significant differences in HR, fR, RT or blood pressures between the two drug combinations. In conscious giraffes, HR of 60–80 beats minute^{-1}, f_R of 8–10 breaths minute^{-1}, body temperature of 38.5 ± 0.5 °C (Mitchell & Skinner 2004), SAP of 140–180 mmHg and DAP of 90–120 mmHg have been reported (Paton et al. 2009). The f_R of 65 breaths minute^{-1} was therefore clinically significantly elevated in these immobilized giraffes with both drug combinations. The development of tachypnoea in giraffe when anaesthetized with a combination of ketamine–medetomidine has been previously reported (Kyoo-tae et al. 2003; Citino et al. 2006; Delk et al. 2019).

Tachypnoea might have developed as a result of severe hypoxemia (PaO_2 < 60 mmHg) which was observed with both drugs combinations. Hypoxaemia is a frequently reported complication in immobilized giraffes, regardless of the drug combination used, when oxygen supplementation or mechanical ventilation is not provided (Vogelnest & Ralph 1997; Delk et al. 2019; Vitali et al. 2020). The $PaCO_2$ values were within or close to normal reference ranges (35–45 mmHg; 4.7–6.0 kPa) for both drug combinations with slight hypocapnia observed in BAM-immobilized animals (33 ± 3 mmHg; 4.4 ± 0.4 kPa). This indicates that ventilation was adequate, and the hypoxaemia likely resulted from ventilation–perfusion mismatch caused by the drugs or the positioning of the animals.

Of clinical relevance is that SpO_2 measurements were above 95% indicated normal oxygen saturation, but the giraffes were hypoxaemic based on arterial blood gas analysis. This disparity between oxygen measures indicates that pulse oximetry, as used in this study, is an unreliable method in giraffe to monitor oxygenation. Similar findings in giraffes have been reported by Bertelsen et al. (2017) who hypothesized that this discrepancy might be caused by a difference between the human and giraffe haemoglobin dissociation curve.

Elevated lactate concentrations, combined with a negative base excess and near-normal $PaCO_2$ values, indicate the presence of metabolic acidosis (Kraut & Madias 2010). Hyperlactataemia probably resulted from stress, muscle exertion during induction and hypoxaemia, all contributing to this acid–base imbalance (Breed et al. 2019). Lactate concentrations of 0.44 ± 0.25 mmol L^{-1} have been reported in zoo giraffes (Cole et al. 2024), highlighting the significance of the elevated lactate values observed with both drug combinations in this study, which indicate clinically relevant hypoxaemia or acid–base disturbances. The observed tachypnoea may have even been a compensatory response to both hypoxaemia and acidaemia. This suggests that compensatory mechanisms remained functional, and hypoventilation was not evident with these drug combinations. Hypoventilation is a common concern when potent opioids are used for immobilizing ungulates (Meyer et al. 2015; Haw et al. 2016).

The limitations of this study were that the order of drug administration was not randomized, and the assessors were not blinded to the identity of the drug combination used. A confounding factor of this study was the need to use two darts to deliver the drug volume, as larger darts were unavailable at the time. However, as both darts were administered in quick succession, the impact of this delay is likely minimal. Additionally, the study was conducted under field conditions and on an opportunistic basis, resulting in a small sample size of only female giraffes. Despite this, the findings provide valuable insights into giraffe immobilization, although we cannot comment on if there would be a different outcome in male or adult giraffes. Some of the giraffes from both drug combinations had hyperthermia which was not treated in this study. However, active cooling measures, such as dousing with water and actively rubbing it in to reach the skin, should be planned for when immobilizing these animals under field conditions (Sawicka et al. 2015, Leiberich et al. 2023). The fasting time in our study was shorter than 24–48 hours, and this could have played a role on the respiratory and metabolic variables whereby the heavy gastrointestinal tract may have compressed the diaphragm, for example. Finally, the dose of

., 52, 403–411

ketamine was fixed regardless of the shoulder height (size) of the giraffes and further research is indicated to refine the ketamine dose in combination with BAM.

Conclusions

In this study, subadult female giraffe were reliably immobilized for at least 30 minutes using either drug combination. KBAM had a faster induction time than BAM. The quality of recovery was calm and coordinated in most of the giraffes regardless of drug combination used. Hypoxaemia and hyperlactatemia occurred with both drug combinations. Therefore, oxygen supplementation should be provided if these drug combinations are used.

Conflict of interest statement

GEZ is an associate editor at the journal *Veterinary Anaesthesia and Analgesia*. JPR and LLL are employed by Wildlife Pharmaceuticals, the source of drugs used in the trial. The remaining authors declare no conflict of interests.

Acknowledgements

We would like to express our sincere gratitude to Wildlife Pharmaceuticals (Pty) Ltd. for their generous funding and invaluable support in facilitating this study. Their commitment to advancing wildlife research and conservation has been instrumental in enabling us to conduct this work. We appreciate their collaboration and expertise, which significantly contributed to the success of our project.

Authors' contributions

SP and LLL: study design, data interpretation, statistical analysis and manuscript drafting. AS, JPR, LLL, LLW and MWM: study design. GEZ and EPB: data interpretation, statistical analysis and manuscript drafting. All authors participated in the data collection and contributed with the manuscript editing.

References

Apps P (2000) Wild Ways: Field Guide to the Behaviour of Southern African Mammals. Struik, South Africa. pp. 1–208.

Bertelsen MF, Grøndahl C, Stegmann GF et al. (2017) Accuracy of noninvasive anesthetic monitoring in the anesthetized giraffe (*Giraffa camelopardalis*). J Zoo Wildl Med 48, 609–615.

Breed D, Meyer LCR, Steyl JCA et al. (2019) Conserving wildlife in a changing world: understanding capture myopathy - a malignant outcome of stress during capture and translocation. Conserv Physiol 7, 1–21.

Bush M, Ensley PK, Mehren K, Rapley W (1976) Immobilization of giraffes with xylazine and etorphine hydrochloride. J Am Vet Med Assoc 169, 884–885.

Bush M, Grobler D, Raath JP et al. (2001) Use of medetomidine and ketamine for immobilization of free-ranging giraffes. J Am Vet Med Assoc 218, 245–259.

Bush M, Grobler DG, Raath JP (2002) The art and science of giraffe (*Giraffa camilopardalis*) immobilization/anesthesia. In: Zoological Restraints and Anesthesia. Heard D (ed.). International Veterinary Information Service publication, USA. pp. 9–14.

Bush M, Vos VD (1987) Observations on field immobilization of free-ranging giraffe (*Giraffa camelopardalis*) using carfentanil and xylazine. J Zoo Anim Med 18, 135–140.

Chittick E, Horne WA, Wolfe B et al. (2012) Cardiopulmonary assessment of medetomidine, ketamine and butorphanol anaesthesia in captive Thomson's gazelles (*Gazella thomsoni*). J Zoo Wildl Med 32, 168–175.

Citino SB, Bush M, Lance WR et al. (2006) Use of thiafentanil (A3080), medetomidine and ketamine for anesthesia of captive and free-ranging giraffe. Proceedings AAZV Conference 211–213.

Cole JE, Dadone L, Rao S et al. (2024) Venous blood gas and lactate values in adult giraffe trained for voluntary jugular phlebotomy. Zoo Biol 43, 371–375.

Dagg AI (2014) Giraffe: Biology, Behaviour and Conservation (2nd edn). Cambridge University Press, UK.

Delk KW, Mama KR, Rao S et al. (2019) Comparison of anesthesia of adult giraffe (*Giraffa camelopardalis*) using medetomidine-ketamine with and without a potent opioid. J Zoo Wildl Med 50, 457–460.

Dittmer M, Haefele H, Swenson J, Heatley JJ (2023) Retrospective comparison of five drug protocols for immobilization of captive sable antelope (*Hippotragus niger*). J Zoo Wildl Med 54, 455–463.

Hansen CM, Beckmen KB (2018) Butorphanol-azaperone-medetomidine for the immobilization of captive caribou (*Rangifer tarandus granti*) in Alaska, USA. J Wildl Dis 54, 650–652.

Harms NJ, Jung TS, Hallock M, Egli K (2018) Efficacy of a butorphanol, azaperone, and medetomidine combination for helicopter-based immobilization of bison (*Bison bison*). J Wildl Dis 54, 819–824.

Haw A, Meyer LCR, Fuller A (2016) Nalbuphine and butorphanol reverse opioid-induced respiratory depression but increase arousal in etorphine-immobilized goats (*Capra hircus*). Vet Anaesth Analg 43, 539–548.

Kraut JA, Madias NE (2010) Metabolic acidosis: pathophysiology, diagnosis and management. Nat Rev Nephrol 6, 274–285.

Kreeger TJ, Arnemo JM, Caulkett NA et al. (2023) Handbook of Wildlife Chemical Immobilization (6th edn). Published by authors, Bovey, USA.

Kyoo-tae K, Jong-bu K, Kyung-cheol C et al. (2003) Chemical immobilization of reticulated giraffe (*Giraffa camelopardis reticulata*) using medetomidine and ketamine. Korean J Vet Res 43, 501–505.

Lamberski N, Newell A, Radcliffe RW (2004) Thirty immobilizations of captive giraffe (*Giraffa camelopardalis*) using a combination of medetomidine and ketamine. In: Proceedings AAZV, AAWV, WDA Joint Conference. pp. 118–120.

Langman VA (1973) The immobilization and capture of giraffe. S Afr J Sci 69, 200–203.

Lapid R, Shilo-Benjamini Y (2015) Immobilization of captive Nubian ibex (*Capra nubiana*) with butorphanol-midazolam-medetomidine or butorphanol-azaperone-medetomidine and atipamezole reversal. J Zoo Wildl Med 46, 291–297.

Leiberich M, Fitte A, Burroughs R et al. (2023) Cooling by dousing with cold water does not alter the pathophysiological biochemical changes induced by capture in blesbok (Damaliscus pygargus phillipsi). J Wildl Dis 59, 288–298.

Meyer LCR, Hetem RS, Mitchell D, Fuller A (2015) Hypoxia following etorphine administration in goats (*Capra hircus*) results more from pulmonary hypertension than from hypoventilation. BMC Vet Res 11, 1–9.

Mich PM, Wolfe LL, Sirochman TM et al. (2008) Evaluation of intramuscular butorphanol, azaperone, and medetomidine and nasal oxygen insufflation for the chemical immobilization of white-tailed deer (*Odocoileus virginianus*). J Zoo Wildl Med 39, 480–487.

Miller BF, Osborn DA, Lance WR et al. (2009) Butorphanol-azaperone-medetomidine for immobilization of captive white-tailed deer. J Wildl Dis 45, 457–467.

Mitchell G, Skinner JD (2004) Giraffe thermoregulation: a review. Transactions of the Royal Society of South Africa 59, 109–118.

Mtetwa TK, Zeiler GE, Laubscher L et al. (2020) Evaluation of the reliability of pulse oximetry, at different attachment sites, to detect hypoxaemia in immobilized impala (*Aepyceros melampus*). Vet Anaesth Analg 47, 323–333.

O'Connor D, Stacy-Dawes J, Muneza A et al. (2019) Updated geographic range maps for giraffe, Giraffa spp., throughout sub-Saharan Africa, and implications of changing distributions for conservation. Mamm Rev 49, 285–299.

Paton JFR, Dickinson CJ, Mitchell G (2009) Harvey Cushing and the regulation of blood pressure in giraffe, rat and man: Introducing "Cushing's mechanism.". Exp Physiol 94, 11–17.

Roeder MM, Bapodra-Villaverde P, Aczm D et al. (2024) Evaluation of thiafentanil-medetomidine-ketamine combinations for anesthesia without the use of a restraint device in adult zoo-housed giraffe (*Giraffa camelopardalis*). In: Proceedings of the Joint AAZV/EAZWV Conference. pp. 107–108.

Sailler A, Potier R, Aczm D, Lécu A (2024) Staged two-dart anesthesia combination of two ultra-potent opioids in captive giraffes (*Giraffa camelopardalis*). In: Proceedings of the AAZV/EAZWV Conference. p. 89, 89.

Sawicka J, Fuller A, Fick LG et al. (2015) Efficacy of different cooling methods for capture-induced hyperthermia in antelope. Afr J Wildl Res 45, 100–110.

Semjonov A, Andrianov V, Raath JP et al. (2018) Evaluation of butorphanol-azaperone-medetomidine (BAM) in captive blesbok immobilization (*Damaliscus pygargus phillipsi*). Vet Anaesth Analg 45, 496–501.

Vitali F, Kariuki EK, Mijele D et al. (2020) Etorphine-azaperone immobilisation for translocation of free-ranging masai giraffes (*Giraffa camelopardalis tippelskirchi*): a pilot study. Animals 10, 1–18.

Vogelnest L, Ralph HK (1997) Chemical immobilisation of giraffe to facilitate short procedures. Aust Vet J 75, 180–182.

Wolfe LL, Fisher MC, Davis TR, Miller MW (2014) Efficacy of a low-dosage combination of butorphanol, azaperone, and medetomidine (BAM) to immobilize rocky mountain elk. J Wildl Dis 50, 676–680.

York W, Kidder C, Durr C (1973) Chemical restraint and castration of an adult giraffe. J Zoo Anima Med 4, 17–21.

Received 8 November 2024; accepted 25 April 2025.

Available online 3 May 2025

