J S Afr Vet Assoc. 2025;96:185-192
https://doi.org/10.36303/JSAVA.674

J S Afr Vet Assoc
ISSN 2224-9435 EISSN 1019-9128

ORIGINAL RESEARCH

Evaluation of immobilisation using a fixed-dose combination of butorphanol, azaperone, and medetomidine, along with a low dose of ketamine, in chacma baboons (*Papio ursinus*)

S Pfitzer,[1] LC Bäckström,[2] JP Raath,[3] A Semjonov,[2] LL Laubscher[3]

[1] *Department of Nature Conservation, Tshwane University of Technology, South Africa*
[2] *Clinical Veterinary Medicine, Institute of Veterinary Medicine and Animal Sciences, Estonian University of Life Sciences, Estonia*
[3] *Wildlife Pharmaceuticals, South Africa*
Corresponding author, email: *silke.pfitzer@icloud.com*

Background: Current literature most commonly describes the use of the dissociative drug ketamine for the immobilisation of baboons, either on its own or in combination with other drugs such as α-2 agonists or benzodiazepines. Currently, no reversal is available for ketamine, leading to prolonged and often rough recoveries of the animals, especially if high doses of ketamine are used.

Objectives: In this study, the fixed-dose combination of butorphanol, azaperone and medetomidine (BAM) with a low dose of ketamine (K-BAM) was evaluated for immobilisation and recovery parameters of chacma baboons.

Methods: Fifteen baboons were immobilised and monitored. Actual doses administered: BAM 0.01 ± 0.005 ml/kg (butorphanol 0.31 ± 0.15 mg/kg, azaperone 0.12 ± 0.06 mg/kg, medetomidine 0.12 ± 0.06 mg/kg) and ketamine 2.04 ± 0.22 mg/kg. During immobilisation, heart rate (HR), respiration rate (RR), peripheral oxygen saturation (SpO_2), end-tidal carbon dioxide ($EtCO_2$), non-invasive blood pressure (BP) and blood gases were evaluated.

Results: Inductions were reached in 3.46 ± 1.36 minutes. Overall, severe hypoxaemia (SpO_2: 62 ± 13%; PaO_2: 37 ± 10 mmHg) was observed in all baboons as well as elevated $EtCO_2$ (63 ± 9 mmHg) and $PaCO_2$ (63 ± 9 mmHg) values. Other measured parameters stayed within normal ranges. Recoveries were fully reached at 4.8 ± 2.8 minutes after intramuscular injection of the reversal naltrexone and atipamezole.

Conclusion: BAM with a low dose of ketamine produced short-term immobilisation, allowing for minor veterinary procedures. The severe hypoxaemia observed in all animals, however, raises serious concerns regarding the safety of this protocol.

Keywords: butorphanol, medetomidine, azaperone, ketamine, primates, chemical immobilisation, baboons

Introduction

Baboons are opportunistic animals that cause safety concerns when encountering human populations upon migration into urban areas (Hoffman & O'Riain 2012). Approaching these animals is challenging as baboons are large and can be extremely aggressive when provoked. Often, they first have to be lured into traps using food before they can be safely immobilised (Isbell et al. 2019). Therefore, chemical immobilisation by remote drug delivery systems is used regularly to ensure both human safety as well as animal welfare. Despite this, there is a paucity of recent information with regards to chemical immobilisation and/or anaesthesia of baboons. Most commonly, the use of dissociative anaesthetics such as ketamine and phencyclidine have been described, either alone or in combination with α-2 agonists and/or benzodiazepines (Melton 1980; Meltzer, Van Vuuren & Bornman 1988; Plooy et al. 1998; Langoi et al. 2009; Isbell et al. 2019). Reported dosages for ketamine in baboons ranged from 10 mg/kg to 32 mg/kg used on its own or for anaesthetic induction (Melton 1980; Du Plooy et al. 1998; Isbell et al. 2019) to 10 mg/kg and 15 mg/kg respectively when combined with an α-2 agonist (Meltzer et al. 1988; Langoi et al. 2009). Although ketamine, as a N-Methyl-D-Aspartate (NMDA) receptor antagonist, is an effective analgesic and anaesthetic, it results in poor muscle relaxation. At this stage, no reversal is available, often resulting in long and rough recoveries from the anaesthetic drug if used in high dosages (Ølberg & Sinclair 2014). Baboon males live in dominance hierarchies and frequently enact aggressive behaviour towards each other as well as towards females (Kalbitzer et al. 2015). This may be problematic when reintroducing not fully recovered animals into the troop, since baboons showing signs of weakness may be bullied or even injured by other troop members. Therefore, reversible or at least partially reversible immobilising agents are preferred.

Medetomidine at 0.1 to 0.2 mg/kg was reported to produce moderate sedation in hamadryas baboons (*Papio hamadryas*) by Jalanka & Roeken (1990). Otherwise, literature on the use of the opioid butorphanol and the α-2 agonist medetomidine in baboons is scarce. Both drugs have been used in other primates, often in combination with ketamine. (Selmi et al. 2004; Lee et al. 2010; Ochi et al. 2014). Ochi et al. (2014) achieved anaesthesia of over 190 minutes duration in cynomolgus monkeys (*Macaca fascicularis*) using the combination of medetomidine (0.015 to 0.04 mg/kg), butorphanol (0.15 to 0.4 mg/kg) and midazolam (0.1 to 0.3 mg/kg). Selmi et al. (2004) achieved anaesthesia in golden-headed lion tamarins (*Leontopithecus chrysomelas*) using a combination of 10 mg/kg ketamine plus 0.02 mg/kg medetomidine while Lee et al. (2010) anaesthetised rhesus

macaques and cynomolgus monkeys with a similar dosage of 3 mg/kg ketamine plus 0.15 mg/kg medetomidine.

Azaperone is a short-acting tranquilliser with no reversal. At present, there is very little known about the effects of azaperone in primates. Meltzer et al. (1988) used a total dose of 20 mg azaperone per chacma baboon (*Papio ursinus*) (approximately 0.5 to 1 mg/kg) in combination with ketamine (15 mg/kg). This seemed to produce sufficient immobilisation to carry out electro-ejaculation on these animals. Low doses of azaperone (up to 0.14 to mg/kg) seemed to have no or little effect on recovery from immobilisation of various wildlife species (Semjonov 2020).

BAM has been used as a reversible immobilisation protocol in a variety of non-domestic species, including rhesus macaques (*Macaca mulatta*) (Wolfe, Goshorn & Baruch-Mordo 2008; Miller et al. 2009; Siegal-Willott et al. 2009; Semjonov et al. 2017; Semjonov et al. 2018; Malinowski et al. 2019; Semjonov et al. 2019). The two BAM dosages reported to produce anaesthesia in rhesus macaques consisted of 0.44 mg/kg butorphanol, 0.15 mg/kg azaperone plus 0.17 mg/kg medetomidine and 0.66 mg/kg butorphanol, 0.22 mg/kg azaperone plus 0.26 mg/kg medetomidine respectively (Malinowski et al. 2019).

To find a safe, reversable immobilisation protocol for free ranging chacma baboons, this study was designed to evaluate the reversable fixed-dose drug combination butorphanol, azaperone and medetomidine (BAM; Wildlife Pharmaceuticals, White River, Mpumalanga, South Africa).

Materials and methods

Most immobilising drugs used in wildlife are compounded by specialist pharmacies and lack official registration for this purpose (Foggin et al. 2021), with no drugs specifically registered for baboons or primates. Even commonly used combinations, like ketamine and medetomidine, generally consist of compounded products or are used off-label. Since the fixed dose BAM combination was not registered for use in primates, ethical approval for the study was sought and granted by the Wildlife Pharmaceuticals Animal Ethics Committee under permit number WPAEC-2018-BAMBABOON-26-B.

The fixed-dose BAM combination investigated in this study consisted of the following active pharmaceutical ingredients: butorphanol (30 mg), azaperone (12 mg) and medetomidine (12 mg) per ml. Based on available literature, initially doses of between 0.0155 and 0.025 ml/kg BAM were used in a dose-titration pilot study on six individually housed captive animals. However, even the comparatively high dose of 0.025 ml/kg BAM which translates into butorphanol 0.75 mg/kg azaperone 0.3 mg/kg and medetomidine 0.3 mg/kg did not lead to full recumbency.

A low dose of ketamine (2 mg/kg) (200 mg/ml, Wildlife Pharmaceuticals, White River, Mpumalanga, South Africa) was therefore added to the BAM protocol to improve induction time and the depth of immobilisation. With this low ketamine dose, a rapid recovery upon reversal of the other agents was still expected. This combination of drugs is hereafter referred to as K-BAM.

Atipamezole (20 mg/ml, Wildlife Pharmaceuticals, White River, Mpumalanga, South Africa) was used intramuscularly to reverse medetomidine at ten times the actual medetomidine mg dose. Although an atipamezole dose of five times the medetomidine dose is recommended for medetomidine reversal in small animals, human and primate data suggests that atipamezole at 10 times the dose may be more appropriate as well as safe in these species (Greenberg, Rama & Zuba 2018). Naltrexone hydrochloride (Trexonil, 50 mg/ml, Wildlife Pharmaceuticals, White River, Mpumalanga, South Africa) was injected intramuscularly to reverse butorphanol at 1 mg of naltrexone per 1 mg of butorphanol. After all physiological measurements for this study were completed and before the animals received the reversal drugs, morphometric measurements were taken from each animal. Therefore, some animals were immobilised for up to 58 minutes in total.

To evaluate the physiological response to BAM (0.025 ml/kg) plus ketamine (2 mg/kg), 15 chacma baboons from Riverside Wildlife Rehabilitation Centre in Limpopo, South Africa, were included for detailed monitoring and evaluation of the immobilisation. The baboons were routinely captured and immobilised in groups for translocation purposes. Animals were baited with food and captured in a secondary, smaller enclosure adjacent and connected to the large enclosure. A Daninject dart gun and Daninject darts (volume 1.5 ml with 1.5 mm x 25 mm needle) (DanInject ApS, Kolding, 6000, Denmark) were used for remote injection. Distance of darting was approximately three to six meters. Drug volumes were based on an estimated weight of the animal. Lowering of the head, ataxic gait, and dropping of the lower jaw were recorded as first signs of sedation. Once recumbent and approachable, each animal was blindfolded and carried to a working area in the shade, where it was weighed, intubated and kept in lateral recumbency throughout the monitoring period. Monitoring started within 15 minutes after darting.

The ambient temperature was noted at the time each baboon was darted. Physiological values were recorded thereafter every five minutes (starting at T0). A total of six measurement points were taken for each baboon. (T0, T5, T10, T15, T20, T25). Animals were extubated once monitoring was complete and just prior to administration of atipamezole and naltrexone intramuscularly. Time elapsed from administering the reversal agents until first signs of recovery as well as full recovery were recorded. First signs of recovery were observed as eye blinking, head lifting, and voluntary limb movements. Full recovery was recorded as the time the baboon was sitting or standing up in the recovery cage.

Anaesthetic depth was evaluated based on palpebral reflex, reaction to painful stimuli (injections) and jaw tone, which was measured as either present or absent. The following parameters were monitored with a veterinary monitor (Mindray, iMEC8 vet, Shenzhen Mindray Bio-electronics Co. Ltd, Nanshan, Shenzhen, 518057, China): heart rate (HR), respiration rate (RR), peripheral oxygen saturation (SpO_2), end-tidal carbon dioxide ($EtCO_2$) and non-invasive blood pressure (BP). Blood pressure was measured by oscillometry with the cuff placed on the upper arm. Circulation and perfusion were evaluated by checking the peripheral pulse

and capillary refill time (CRT). The probe for measuring oxygen saturation was attached to the tongue. Auscultation of the heart was done with a stethoscope and a digital thermometer was used to measure rectal temperature (RT).

Arterial blood was obtained from either the femoral artery or the caudal tail artery for blood gas analysis. Blood was collected using a 23G needle and a heparinised 1 ml syringe. Three samples were collected at T0, T10, T20 of monitoring. The samples were immediately analysed using a portable analyser (EPOC Reader Blood Analysis and EPOC BGEM smart cards; Epocal; Kyron Laboratories, Johannesburg, 2094, Gauteng, South Africa). The following parameters were evaluated: blood pH, arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$) and lactate.-

For the analysis of anaesthetic effects, HR, RT, RR, systolic BP (SBP), diastolic BP (DBP) and mean BP (MBP), SpO_2, PaO_2, $PaCO_2$, pH and lactate, the area under the curve (AUC) was calculated using a trapezoid method for every measurement for the immobilisation monitoring period. The mean AUCs were used as response variables in linear regression models. The given dose of K-BAM (based on weighing the animal once immobilised) was categorised into three groups: low (D1, $n = 5$): 0.0067–0.0079 ml/ kg, medium (D2, $n = 6$): 0.0080–0.0099 ml/ kg, high (D3, $n = 4$): ≥ 0.01 ml/ kg) and used as a categorical explanatory variable. D1 consisted of three females (one adult and two sub-adults) and two males (one adult and one sub-adult), D2 consisted of two females (one adult and one sub-adult) and four males (three adults and one sub-adult) and D3 consisted of one female (an adult) and three males (all adults). Age (divided into two levels: sub-adult [< 15 kg] and adult [> 15 kg]) (Smithers 2012) and gender were used as categorical explanatory variables. Weight of the animals and ambient temperature were used as continuous explanatory variables. For analysing the effect of K-BAM on induction time (recumbency) and recovery time, similar linear regression models were used with K-BAM dose, age, and gender as categorical explanatory variables. A p-value of ≤ 0.05 was considered as statistically significant. Data is reported as mean ± standard deviation (range). For all models, STATA 14.0 (Stata Corporation, Texas, USA) statistical software was used.

Results

Six female baboons (16.1 ± 2.7 kg, range 12.5–19.9 kg, three sub-adults, three adults) and nine male baboons (22 ± 8.9 kg, range 6.7–38 kg, two sub-adults, seven adults) were immobilised with the K-BAM protocol. The actual dose injected was 0.01 ± 0.005 ml/kg BAM (butorphanol 0.31 ± 0.15 mg/kg, azaperone 0.12 ± 0.06 mg/kg, medetomidine 0.12 ± 0.06 mg/kg) plus 2.03 ± 0.22 mg/kg ketamine.

All baboons injected with K-BAM were successfully immobilised after a single injection and had smooth and calm inductions. First signs of sedation were observed after 1.86 ± 0.70 minutes. All animals were recumbent after 3.46 ± 1.36 minutes and fully recovered within 4.80 ± 2.80 minutes after injection of the reversal agents.

Eleven animals displayed adequate muscle relaxation throughout the monitoring period, four animals exhibited mild jaw tone at the start of monitoring. Palpebral reflexes were either absent or weak. CRT was less than two seconds in all animals throughout the immobilisation. None of the baboons showed reactions to blood sampling.

Thirteen baboons stayed immobilised until receiving reversal agents. One male and one female showed signs of recovery after 42 and 49 minutes after darting prior to the reversal agents being administered. These events happened after all measuring points had been taken and animals were excluded from the analysis of recovery.

Physiological parameters measured are illustrated in Table I.

The ambient temperature in between immobilisations varied from 20 to 32 °C (25.2 ± 3.2 °C). Higher ambient temperature resulted in higher RT ($R^2 = 0.685$, $p = 0.002$) as well as higher lactate levels ($R^2 = 0.444$, $p = 0.009$) at the start of the

Table I: Physiological response of 15 baboons during a 40-minute period, whilst being immobilised with K-BAM. All quantitative values are expressed as the mean ± standard deviation (SD) with overall minimum–maximum range.

Variable	T0	T10	T20	Overall (min-max)
HR (beats/minute)	96.8 ± 18.8	90.7 ± 20.2	86.5 ± 18.5	54.0–133.0
RR (breaths/minute)	28.8 ± 9.7	27.3 ± 8.2	27.2 ± 8.6	11.0–47.0
RT (°C)	39.0 ± 0.7	38.6 ± 0.7	38.6 ± 0.8	37.1–40.7
SBP (mmHg)	103.8 ± 7.6	101.9 ± 7.4	98.5 ± 6.3	86.0–118.0
DBP (mmHg)	58.1 ± 11.0	59.7 ± 9.4	56.6 ± 8.3	34.0–78.0
MBP (mmHg)	73.6 ± 8.6	74.2 ± 8.6	69.9 ± 8.8	51.0–91.0
SpO_2 (%)	56.9 ± 12.7	60.8 ± 13.1	68.3 ± 12.9	33.0–94.0
$EtCO_2$ (mmHg)	60.0 ± 9.2	63.7 ± 8.5	63.2 ± 8.7	44.0–82.0
PaO_2 (mmHg)	35.1 ± 7.3	37.2 ± 10.5	41.3 ± 10.9	20.0–64.0
$PaCO_2$ (mmHg)	60.2 ± 8.5	62.4 ± 8.7	65.3 ± 9.1	46.3–80.1
pH	7.3 ± 0.04	7.3 ± 0.04	7.3 ± 0.04	7.2–7.37
Lac (mmol/l)	2.1 ± 1.9	1.3 ± 1.0	1.1 ± 0.7	0.5–8.1

HR, heart rate; RR, respiratory frequency; RT, rectal temperature; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; SpO_2, haemoglobin oxygen saturation; $EtCO_2$, end-tidal carbon dioxide; PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide. T0 is the time of the first measurement which was collected 15 minutes after darting.

immobilisation. Both values decreased significantly during the monitoring period ($p < 0.001$ for both). No significant changes in arterial blood pH during immobilisation could be observed over time (Table I).

Mean HR ranged from 96.8 ± 18.8 at T0 to 86.5 ± 18.5 beats/minute at T20. No apnoea was observed in any of the baboons and RR stayed relatively stable between 28.8 ± 9.7 and 27.2 ± 8.6 breaths per minute.

Despite the stable RR, all animals were severely hypoxaemic (PaO_2 < 60 mmHg and SPO_2 < 90%) (Grimm et al. 2015). Hypoxaemia was combined with hypercapnia as $EtCO_2$ values of up to 63.7 ± 8.5 mmHg and $PaCO_2$ values up to 65.3 ± 9.1 mmHg were measured (Table I). Respiration was reported as being shallow.

Blood pressure values were stable throughout the measuring period (Table I).

After transportation to the release site, the animals were remotely monitored for several days, and no mortalities or morbidities were reported.

Discussion

The present study indicates that K-BAM at a dose of 0.025 ml/kg of BAM with 2.0 mg/kg of ketamine can result in complete immobilisation of chacma baboons. At this dose, the earliest sign of spontaneous awakening was observed at 42 minutes after darting, at which time the effect of ketamine would have been minimal considering the low dose and the relatively fast elimination time of ketamine (Mion & Villevieille 2013).

Rectal temperature declined over time. The normal RT of primates has been reported as 37–39.5 °C which means that RT in this study fell within an acceptable range (Laffins et al. 2017). Initially mildly elevated RTs (39.0 ± 0.7 °C) were found to be correlated to elevated ambient temperatures ($R^2 = 0.685$, $p = 0.002$). Additionally, high excitement and stress responses could have contributed to these initially elevated RTs (Meyer 2009; Breed et al. 2019). As immobilisation progressed and animals were monitored in a shaded area, the reduction in stress possibly led to the decline in RT. Lactate values of 2.1 ± 1.9 mmol/l at T0 would have to be regarded as slightly above normal reference values of up to 2.0 mmol/l reported for monkeys by Hobbs et al. (2010) which could explain the mild acidosis (pH 7.3 ± 0.04) observed throughout the measuring period (Hobbs et al. 2010).

Cardiovascular parameters appeared stable in all animals. The HR of between 86.5 and 96.8 beats per minute is similar to values of between 90 and 110 beats per minute reported in habituated baboons by Brent & Weaver (1996). The same authors also reported a MBP of 90 to 96 mmHg, which is slightly higher than the MBP measured in baboons immobilised with K-BAM (69.9 to 74.2 mmHg).

All parameter changes listed so far are not of significant clinical relevance and would allow for K-BAM to be evaluated as a suitable anaesthetic for baboons. However, this might have been deceiving. It could be hypothesised that the severe hypoxaemia should have triggered tachycardia (Kane, Kothmann & Giussani 2020). However, medetomidine is known to cause bradycardia and when combined with butorphanol it can also lead to hypotension in some primates (Kalema-Zikusoka et al. 2003; Lee et al. 2010; Larsen, Sauther & Cuozzo 2011; Malinowski et al. 2019). Therefore, these drug effects might have masked tachycardia which would have physiologically developed in response to hypoxaemia.

All animals were severely hypoxaemic (PaO_2 < 60 mmHg), indicating the detrimental effects on respiration and gas exchange of this combination (Grimm et al. 2015). Butorphanol has shown to produce significant decreases in oxygen saturation in a variety of primate species. In rhesus monkeys, respiratory depression was seen in doses ranging from 0.001–0.32 mg/kg (Butelman et al. 1995). In the same species, the minute volume of respiration decreased to one third of control values when butorphanol was given at a dose of 0.3 mg/kg (Liguori, Morse & Bergman 1996). Medetomidine is also known to have an inhibitory effect on the cardiopulmonary system, causing a decrease in RR, especially in combination with other sedatives (Sinclair 2003). In rhesus monkeys immobilised with BAM, a low oxygen saturation was explained as a result of the vasoconstriction induced by medetomidine (Malinowski et al. 2019). It is hypothesised that both medetomidine and butorphanol contributed to the respiratory compromise seen in the current study.

Hypercapnia could indicate that hypoventilation played a part in the development of hypoxaemia. A lack in physiological response to counteract high $EtCO_2$ and $PaCO_2$ was evident, as there was no stimulation of respiration. Although no apneustic-type breathing was observed, breathing did appear to be quite shallow. The decreased sensitivity to increased CO_2 levels may be explained by butorphanol's action on μ-opioid receptors within the CNS, including the areas in the pons (pre-Bötzinger complex) responsible for regulating respiratory rhythm (Butelman et al. 1995; Liguori et al. 1996; Boom et al. 2012). However, a ventilation perfusion mismatch or other reasons for hypoxaemia in addition to hypoventilation cannot be excluded based on the available data. In this field study, the respiratory minute volume was not measured. Barometric pressures were not recorded which would allow for a calculation of the Alveolar–arterial oxygen (A-a) gradient and thus further explain the origin for hypoxaemia (Sarkar, Niranjan & Banyal 2017). This study was designed to simulate real-world field conditions, where oxygen supplementation is typically not available. As such, no provisions for routine oxygen supplementation were made. In hindsight, endpoints should have been established based on the severity of hypoxaemia, at which point oxygen supplementation should have been implemented. Further short comings of this study were the small number of study subjects of various ages and mixed sex due to the opportunistic nature of this project. The fact that weight estimates before darting of the animals varied widely from the actual weights of the animals, required the introduction of three dose groups into the statistical analysis.

The aim of the study was to evaluate the suitability of K-BAM for the immobilisation of baboons. Despite the fact that K-BAM at the given dose achieved suitable plane of immobilisation for 40 minutes with seemingly stable RR, HR and RT and was fully reversible, it cannot be recommended for the routine use

under field conditions due to the severe hypoxaemia observed during this investigation. If the use of the K-BAM protocol is considered, animals should be closely monitored and oxygen supplementation should be part of the protocol to ensure the safety of the immobilised baboons.

Conclusion

Although the K-BAM combination did result in smooth inductions and quick recoveries and animals could be safely handled and monitored for more than 40 minutes, severe hypoxaemia makes this protocol extremely unsafe for chacma baboons. K-BAM should therefore not be considered as safe or superior to other protocols and further research is required to find fully reversible immobilisation protocols for baboons.

Acknowledgements

We thank the Centre for Animal Rehabilitation and Education (C.A.R.E.) and Riverside Wildlife Rehabilitation Centre, for allowing us to work with their animals.

Conflict of interest statement

The authors declare that they have no conflict of interest directly or indirectly related to the research; except for:

JPR is the director of Wildlife Pharmaceuticals South Africa; a company which develops, produces and sells various wildlife anaesthetics, amongst others the combinations anaesthetic BAM.

Funding sources

This study was financially supported by Wildlife Pharmaceuticals.

Compliance with ethical guidelines

The authors declare that this submission is in accordance with the principles laid down by the Responsible Research Position Statement as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.

Prior to commencement of the study ethical approval was obtained from the following ethical review board: Wildlife Pharmaceuticals (Pty) Ltd Animal Ethics Committee (AEC Approval number: WPAEC-2018-BAMBABOON-26-B).

ORCID

S Pfitzer https://orcid.org/0000-0001-8119-3999
LC Bäckström https://orcid.org/0000-0002-5114-1036
JP Raath https://orcid.org/0000-0001-5083-4386
A Semjonov https://orcid.org/0009-0006-0450-8655
LL Laubscher https://orcid.org/0000-0002-5982-2653

References

Boom, M., Niesters, M., Sarton, E., et al., 2012, Non-analgesic effects of opioids: Opioid-induced respiratory depression, *Current Pharmaceutical Design* 18(37), 5994-6004. https://doi.org/10.2174/138161212803582469.

Breed, D., Meyer, L.C.R., Steyl, J.C.A., et al., 2019, Conserving wildlife in a changing world: Understanding capture myopathy - A malignant outcome of stress during capture and translocation, *Conservation Physiology* 7(1), 1-21. https://doi.org/10.1093/conphys/coz027.

Brent, L., Weaver, O., 1996, The physiological and behavioral effects of radio music on singly housed baboons, *Journal of Medical Primatology* 25(5), 370-374. https://doi.org/10.1111/j.1600-0684.1996.tb00031.x.

Butelman, E.R., Winger, G., Zernig, G., et al., 1995, Butorphanol: Characterization of agonist and antagonist effects in rhesus monkeys, *The Journal of Pharmacology and Experimental Therapeutics* 272(2), 845-853. https://doi.org/10.1016/S0022-3565(25)24501-3.

Foggin, C., Masterson, C., Hoare, R., et al., 2021, Legal and ethical considerations in the use of immobilising drugs, using Namibia, South Africa and Zimbabwe as examples, in M.D. Kock & R. Burrough (eds.), Chemical and Physical Restraint of African Wild Animals, Third Edition, pp. 1-11, Michael D. Kock, Greyton.

Greenberg, M., Rama, A., Zuba, J.R., 2018, Atipamezole as an emergency treatment for overdose from highly concentrated alpha-2 agonists used in zoo and wildlife anesthesia, *American Journal of Emergency Medicine* 36(1), 136-138. https://doi.org/10.1016/j.ajem.2017.06.054.

Grimm, K.A., Lamont, L.A., Tranquilli, W.J., et al., 2015, Veterinary Anesthesia and Analgesia - The fifth edition of Lumb and Jones, Fifth, Wiley- Blackwell: Ames, Iowa. https://doi.org/10.1002/9781119421375.

Hobbs, T.R., O'Malley, J.P., Khouangsathiene, S., et al., 2010, Comparison of lactate, base excess, bicarbonate, and pH as predictors of mortality after severe trauma in rhesus macaques (Macaca mulatta), *Comparative Medicine* 60(3), 233-239.

Hoffman, T.S., O'Riain, M.J., 2012, Monkey management: Using spatial ecology to understand the extent and severity of human-baboon conflict in the Cape Peninsula, South Africa, *Ecology and Society* 17(3). https://doi.org/10.5751/ES-04882-170313.

Isbell, L.A., Bidner, L.R., Omondi, G., et al., 2019, Capture, immobilization, and global positioning system collaring of olive baboons (Papio anubis) and vervets (Chlorocebus pygerythrus): Lessons learned and suggested best practices, *American Journal of Primatology* 81(6). https://doi.org/10.1002/ajp.22997.

Jalanka, H.H., Roeken, B.O., 1990, The use of medetomidine, medetomidine-ketamine combinations, and atipamezole in nondomestic mammals: a review, *Journal of Zoo and Wildlife Medicine* 21(3), 259-282.

Kalbitzer, U., Heistermann, M., Cheney, D., et al., 2015, Social behavior and patterns of testosterone and glucocorticoid levels differ between male chacma and Guinea baboons, *Hormones and Behavior* 75, 100-110. https://doi.org/10.1016/j.yhbeh.2015.08.013.

Kalema-Zikusoka, G., Horne, W.A., Levine, J. et al., 2003, Comparison of the cardiorespiratory effects of medetomidine-butorphanol-ketamine and medetomidine-butorphanol-midazolam in patas monkeys (Erythrocebus patas), *Journal of Zoo and Wildlife Medicine* 34(1), 47-52. https://doi.org/10.1638/1042-7260(2003)34[0047:COTCEO]2.0.CO;2.

Kane, A.D., Kothmann, E., Giussani, D.A., 2020, Detection and response to acute systemic hypoxia, *BJA Education* 20(2), 58-64.

Laffins, M.M., Mellal, N., Almlie, C.L., et al., 2017, Evaluation of infrared thermometry in cynomolgus macaques (Macaca fascicularis), *Journal of the American Association for Laboratory Animal Science* 56(1), 84-89.

Langoi, D.L., Mwethera, P.G., Abelson, K.S.P., et al., 2009, Reversal of ketamine/xylazine combination anesthesia by Atipamezole in olive baboons (Papio anubis), *Journal of Medical Primatology* 38(6), 404-410. https://doi.org/10.1111/j.1600-0684.2009.00378.x.

Larsen, R.S., Sauther, M.L., Cuozzo, F.P., 2011, Evaluation of modified techniques for immobilization of wild ring-tailed lemurs (Lemur catta), *Journal of Zoo and Wildlife Medicine* 42(4), 623-633. https://doi.org/10.1638/2011-0004.1.

Lee, V.K., Flynt, K.S., Haag, L.M., et al., 2010, Comparison of the effects of ketamine, ketamine-medetomidine, and ketamine-midazolam on physiologic parameters and anesthesia-induced stress in rhesus (Macaca mulatta) and cynomolgus (Macaca fascicularis) macaques, *Journal of the American Association for Laboratory Animal Science* 49(1), 57-63.

Liguori, A., Morse, W.H., Bergman, J., 1996, Respiratory effects of opioid full and partial agonists in rhesus monkeys, *Journal of Pharmacology and Experimental Therapeutics* 277(1). https://doi.org/10.1016/S0022-3565(25)12844-9.

Malinowski, C.M., Cameron, A.I., Burnside, W.M., et al., 2019, Butorphanol-azaperone-medetomidine for the immobilization of rhesus macaques (Macaca mulatta), *Journal of the American Association for Laboratory Animal Science* 58(3), 346-355. https://doi.org/10.30802/AALAS-JAALAS-18-000088.

Melton, D.A., 1980, Baboon (Papio ursinus) capture using a blow-dart system, *South African Journal of Wildlife Research* 10(2), 67-70.

Meltzer, D., Van Vuuren, M., Bornman, M.S., 1988, The suppression of electro-ejaculation in the chacma baboon (Papio ursinus) by azaperone, *Journal of the South African Veterinary Association* (1), 53.

Meyer, L.C.R., 2009, Reduction of capture-induced hyperthermia and respiratory depression in ungulates - PhD thesis, University of the Witwatersrand .

Miller, B.F., Osborn, D.A., Lance, W.R., et al., 2009, Butorphanol-azaperone-medetomidine for immobilization of captive white-tailed deer, *Journal of Wildlife Diseases* 45(2), 457-467. https://doi.org/10.7589/0090-3558-45.2.457.

Mion, G., Villevieille, T., 2013, Ketamine pharmacology: an update (pharmacodynamics and molecular aspects, recent findings), *CNS Neuroscience and Therapeutics* 19(6), 370-380. https://doi.org/10.1111/cns.12099.

Ochi, T., Nishiura, I., Tatsumi, M., et al., 2014, Anesthetic effect of a combination of medetomidine-midazolam-butorphanol in cynomolgus monkeys (Macaca fascicularis), *The Journal of Veterinary Medical Science* 76(6), 917-21. https://doi.org/10.1292/jvms.13-0589.

Ølberg, R.A., Sinclair, M., 2014, Monkeys and Gibbons, in G. West, D. Heard & N. Caulkett (eds.), Zoo animal and wildlife immobilization and anesthesia, 2nd Edition, pp. 375-386, Blackwell Publishing, Iowa, USA. https://doi.org/10.1002/9780470376478.ch32.

Plooy, W.J., Schutte, P.J., Still, J., et al., 1998, Stability of cardiodynamic and some blood parameters in the baboon following intravenous anaesthesia with ketamine and diazepam, *Journal of the South African Veterinary Association* 69(1), 18-21. https://doi.org/10.4102/jsava.v69i1.803.

Sarkar, M., Niranjan, N., Banyal, P.K., 2017, Mechanisms of hypoxemia, *Lung India* 34(1), 47-60. https://doi.org/10.4103/0970-2113.197116.

Selmi, A.L., Mendes, G.M., Figueiredo, J.P., et al., 2004, Comparison of medetomidine-ketamine and dexmedetomidine-ketamine anesthesia in golden-headed lion tamarins, *Canadian Veterinary Journal* 45, 481-485.

Semjonov, A., 2020, Evaluation of a fixed-dose combination of butorphanol-azaperone-medetomidine (BAM) for chemical immobilisation of African lion, blesbok, and cheetah - PhD thesis, Estonian University of Life Sciences.

Semjonov, A., Andrianov, V., Raath, J.P., et al., 2018, Evaluation of butorphanol-azaperone-medetomidine (BAM) in captive blesbok immobilization (Damaliscus pygargus phillipsi), *Veterinary Anaesthesia and Analgesia* 45, 496-501. https://doi.org/10.1016/j.vaa.2017.03.011.

Semjonov, A., Andrianov, V., Raath, J.P., et al., 2017, Evaluation of BAM (butorphanol-azaperone-medetomidine) in captive African lion (Panthera leo) immobilization, *Veterinary Anaesthesia and Analgesia* 44(4), 883-889. https://doi.org/10.1016/j.vaa.2017.02.001.

Semjonov, A., Raath, J.P., Laubscher, L.L., et al., 2019, Evaluation of butorphanol-azaperone-medetomidine (BAM) in captive cheetah (Acinonyx jubatus) immobilization, *Veterinary Anaesthesia and Analgesia* 46(1), 90-95. https://doi.org/10.1016/j.vaa.2018.09.038.

Siegal-Willott, J., Citino, S.B., Wade, S., et al., 2009, Butorphanol, azaperone, and medetomidine anaesthesis in free-ranging white-tailed deer (Odocoileus virginianus) using radiotransmitter darts, *Journal of Wildlife Diseases* 45(2), 468-480. https://doi.org/10.7589/0090-3558-45.2.468.

Sinclair, M.D., 2003, A review of the physiological effects of alpha 2-agonists related to the clinical use of medetomidine in small animal practice, *Canadian Veterinary Journal* 44, 885-897.

Smithers, R.HN., 2012, Smithers Mammals of Southern Africa, Penguin Random House, Pretoria, South Africa.

Wolfe, L.L., Goshorn, C.T., Baruch-Mordo, S., 2008, Immobilization of black bears (Ursus americanus) with a combination of butorphanol, azaperone, and medetomidine, *Journal of Wildlife Diseases* 44(3), 748-752. https://doi.org/10.7589/0090-3558-44.3.748.