SHORT COMMUNICATION

Immobilization of captive Persian fallow deer (*Dama dama mesopotamica*) using medetomidine–ketamine or medetomidine–midazolam

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Abstract

Objective To establish and compare the effectiveness of two medetomidine-based immobilization protocols in Persian fallow deer (*Dama dama mesopotamica*).

Study design Prospective, randomized, blinded clinical study.

Animals A group of 31 captive Persian fallow deer.

Methods Deer scheduled for translocation were immobilized with a combination of medetomidine (76 ± 11 μg kg^{-1}) and ketamine (1.0 ± 0.2 mg kg^{-1}) (MK; $n = 15$) or medetomidine (77 ± 11 μg kg^{-1}) and midazolam (0.10 ± 0.01 mg kg^{-1}) (MM; $n = 16$) administered intramuscularly. An observer unaware of group assignments recorded times to immobilization and recovery, monitored physiologic variables and scored the quality of induction, immobilization and recovery (scale 1–5: 1, poor; 5, excellent). Atipamezole was administered for reversal. Data analysis was performed using the *t* test, the Mann–Whitney *U* test, the chi-square test and the Fisher's exact test. Significance was set at $p < 0.05$.

Results Data are presented as mean ± standard deviation or median (range). Time to induce immobilization was 9 ± 4 and 10 ± 4 minutes in the MK and MM groups, respectively. Immobilization quality score was 5 (1–5) following both combinations. Hemoglobin oxygen saturation (SpO_2) was significantly lower in the MK (80 ± 8%) than in the MM group (87 ± 8%) although respiratory frequency did not differ between MK and MM (11 ± 5 and 10 ± 2 breaths $minute^{-1}$, respectively). Recovery times were 13 ± 6 (MK) and 14 ± 7 minutes (MM) and did not differ between groups. No morbidities or mortalities were recorded during 1 month after immobilization.

Conclusions and clinical relevance The MK and MM combinations produced sufficient immobilization in captive Persian fallow deer for short nonpainful procedures. Based on the SpO_2 values, the MM combination may be associated with less respiratory depression; nevertheless, both combinations may result in a decrease in SpO_2.

Keywords *Dama dama mesopotamica*, immobilization, ketamine, medetomidine, midazolam, Persian fallow deer.

Introduction

The Tisch Family Zoological Gardens in cooperation with the Israel Nature and Parks Authority (INPA) conducts breeding and reintroduction of the Persian fallow deer (*Dama dama mesopotamica*) back to Israeli fauna. A reliable and safe immobilization protocol, which is quickly reversible, is required for translocation of the deer to the wild.

Opioids, such as etorphine or thiafentanil, have been used to immobilize Persian fallow deer; however, these drugs are associated with long periods of apnea, and a decrease in hemoglobin oxygen saturation (SpO_2) is common (Lapid et al. 2017). Combinations of α_2-adrenergic receptor agonists and *N*-methyl-D-aspartate (NMDA) receptor antagonists have been used for immobilization of fallow deer (*Dama dama*) (Costa et al. 2017). Medetomidine is a potent and selective α_2-agonist commonly used in combination with the NMDA-antagonist ketamine for immobilization of deer species (Arnemo et al. 2011). Midazolam is a water-soluble benzodiazepine that produces a sedative effect via action on the γ-aminobutyric acid receptor. Advantages associated with midazolam include muscle relaxation, anticonvulsant properties, minimal cardiopulmonary effects and reversibility (Rankin 2015).

The goals of this study were to evaluate medetomidine-based nonopioid combinations with ketamine or midazolam,

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and compare the qualities of induction, immobilization and recovery, physiological variables and occurrence of complications in captive Persian fallow deer. Our hypothesis was that the combinations medetomidine–ketamine and medetomidine–midazolam would provide immobilization sufficient for performing nonpainful procedures.

Materials and methods

All procedures received approval from the INPA and the Institutional Animal Care and Use Committee of the Hebrew University of Jerusalem (MD-14-14127-2). Deer were born in captivity and were habituated to the keepers entering the enclosure with food, but would run away when approached. The deer were housed in an outdoor enclosure of approximately 5000 m^2, and were not fasted prior to darting. Immobilizations were required to transport deer from the breeding center to national parks. A group of 31 deer scheduled for translocation were assigned randomly (https://www.random.org/lists/) to group MK, medetomidine (target dose 100 μg kg^{-1}; 20 mg mL^{-1}; Kyron Laboratories, South Africa) with ketamine hydrochloride (target dose 1.3 mg kg^{-1}; Ketamidor, 100 mg mL^{-1}; Richter Pharma AG, Austria; $n = 15$), or group MM, medetomidine (target dose 100 μg kg^{-1}) with midazolam (target dose 0.13 mg kg^{-1}; 50 mg mL^{-1}; Kyron Laboratories; $n = 16$).

At each capture event, four to six deer were immobilized and each deer was recovered before darting the next. The ambient temperature was recorded and deer weights estimated. The drugs were combined in a 1.5 mL dart syringe with a 1.5 mm, 30 mm plain needle (DAN-INJECT, Denmark) and administered into the hindquarter or shoulder muscle using a CO_2 injection rifle (Model J.M.SP.; DAN-INJECT) fired from a pedestrian bridge that crosses the deer enclosure (approximately 10–15 m distance). If immobilization was not adequate within 15 minutes, then half the dose of the same combination was administered. Following capture, the deer was blindfolded and transported within 5 minutes using an electric vehicle to the enclosure entrance, where all treatments and measurements were performed. Here, the deer was weighed (Electronic scale, MD-900; Bolet Industries Ltd., Israel) and placed in sternal recumbency. The deer was administered a rabies vaccine, treated against endo- and ectoparasites using ivermectin (Noromectin, 10 mg mL^{-1}; Norbrook Laboratories Ltd., Ireland) and the presence of a microchip was verified or one was placed.

Recorded time periods were: time to immobilization (onset), from darting until recumbency; immobilization time, from recumbency until atipamezole administration; and recovery time, from atipamezole administration until standing. Induction, immobilization and recovery qualities were subjectively scored: 1, poor; 2, fair; 3, good; 4, very good; 5, excellent (Appendix A).

During recumbency, heart rate (HR, using a stethoscope), respiratory frequency (counting thoracic movements), rectal temperature (RT, using a digital thermometer), SpO_2 using a probe on the tongue and oscillometric noninvasive mean arterial pressure (MAP) with the cuff (pediatric number 5) placed around the metatarsus (SpO_2 and MAP: MEC-1200Vet; Shenzhen Mindray Bio-Medical Electronics Co. Ltd, GD, China). Variables were measured every 5–10 minutes. All assessments and measurements were performed by an observer unaware of group assignment (BZ).

When all treatments were completed, the deer was placed in a padded transport box and atipamezole (Atipam, 5 mg mL^{-1}; Eurovet Animal Health, The Netherlands) was administered intramuscularly (IM) at five times the medetomidine dose. Transport was in accordance with the guidelines of the International Air Transport Association (Live Animals Regulation). The deer were transported to enclosures in which they were acclimatized for at least a month before being released into the wild.

Statistical analysis

Data analysis was carried out using SPSS Statistics, Version 20.0 (IBM Corporation, NY, USA). Quantitative variables were compared with a t test. When data were not normally distributed then the Mann–Whitney U nonparametric test was applied for comparison between groups. Qualitative variables were compared with the chi-square test and the Fisher's exact test. Significance was set at $p < 0.05$.

Results

Once recumbent, all deer were approachable and none struggled during the procedure. The deer were aged 0.9–5.6 years and weighed 42.0–134.0 kg. Deer data, drug doses, time periods and quality scores were not significantly different between groups (Table 1). Two deer, one of each group, had to be darted twice owing to partial administration on the first attempt; their doses were not included in the table because the exact administered dose was unknown, but all other measured variables were included. In the remaining deer, dose ranges were medetomidine (56–92 μg kg^{-1}) and ketamine (0.7–1.3 mg kg^{-1}) or midazolam (0.08–0.12 mg kg^{-1}; Table 1). Two physiologic variables were averaged per deer for the analysis, and were recorded at 14.3 ± 2.3 and 14.8 ± 2.7 minutes following drug administration in MK and MM, respectively. Mean SpO_2 was significantly higher in MM (87 ± 8%; range 71–99) than in MK (80 ± 8%; range 64–90; $p = 0.025$; Table 1). No other differences occurred in physiologic variables (Table 1).

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Table 1 Data (mean ± standard deviation), drug doses (all administered intramuscularly), time periods, physiologic variables (recorded approximately 15 minutes following drug administration; n = number of deer) and median (range) of induction, immobilization and recovery quality scores (score 1, poor; 5, excellent) of Persian fallow deer immobilized with medetomidine–ketamine (MK; $n = 15$) or medetomidine–midazolam (MM; $n = 16$). One deer in each group required additional drugs; therefore, their drug doses are not included

Variable	Group	
	MK	MM
Number of male:female	9:6	6:10
Age (years)	2.5 ± 1.2	2.6 ± 1.5
Weight (kg)	70.5 ± 25.4	67.5 ± 18.6
Ambient temperature (°C)	13.5 ± 2.6	14.9 ± 2.3
Medetomidine (μg kg^{-1})	76 ± 11 ($n = 14$)	77 ± 11 ($n = 15$)
Ketamine (mg kg^{-1})	1.0 ± 0.2 ($n = 14$)	–
Midazolam (mg kg^{-1})	–	0.10 ± 0.01 ($n = 15$)
Atipamezole (μg kg^{-1})	380 ± 50	400 ± 50
Time to induce immobilization (onset; minutes)	9 ± 4	10 ± 4
Duration of immobilization (minutes)	19 ± 4	21 ± 5
Recovery time (minutes)	13 ± 6	14 ± 7
HR (beats minute^{-1})	50 ± 11 ($n = 14$)	47 ± 13 ($n = 16$)
f_R (breaths minute^{-1})	11 ± 5 ($n = 15$)	10 ± 2 ($n = 15$)
RT (°C)	37.5 ± 0.8 ($n = 13$)	37.6 ± 0.8 ($n = 16$)
MAP (mmHg)	93 ± 23 ($n = 12$)	102 ± 16 ($n = 13$)
SpO_2 (%)	80 ± 8 ($n = 14$)	87 ± 8 ($n = 14$)*
85–99% (n)	5	10
60–84% (n)	9	4
Induction quality (1–5)	5 (1–5)	5 (1–5)
Immobilization quality (1–5)	5 (3–5)	5 (3–5)
Recovery quality (1–5)	4.5 (1–5)	5 (3–5)

HR, heart rate; f_R, respiratory frequency; RT, rectal temperature; MAP, mean arterial pressure; SpO_2, hemoglobin oxygen saturation.
*Significant difference between groups ($p < 0.05$).

All deer recovered without complications from immobilization and were translocated. No morbidities or mortalities were recorded in the month following immobilization prior to the deer being released into the wild.

Discussion

The combinations MK and MM provided smooth immobilization and recovery in the captive Persian fallow deer; however, there were no differences in most measured variables between the groups. The doses used in this study were based on a preliminary study by the authors. The actual doses of MM and MK administered were approximately 25% lower than the target doses as a result of underestimation of the body weight of the deer. Doses of 130 μg kg^{-1} and 3 mg kg^{-1} (Evans et al. 2013), or 210 μg kg^{-1} and 1 mg kg^{-1} (Arnemo et al. 2011) for MK, respectively, have been recommended for Norwegian reindeer (*Rangifer tarandus tarandus*). These higher dose requirements may be attributed to their free-ranging habitat *versus* the captive fallow deer in the present study. The differences in doses among studies may be influenced by different end points, such as anesthetic depth. The authors are not aware of any published doses of MM in deer species.

The onset time to immobilization in both groups was longer than the median induction time of 4.2 minutes reported for MK when combined with tiletamine–zolazepam in white-tailed deer (*Odocoileus virginianus*) (Muller et al. 2012a). In fallow deer immobilized with xylazine–tiletamine–zolazepam, the induction time was approximately 8 minutes (Costa et al. 2017), slightly shorter than induction times in the present study, and may be attributed to the tiletamine–zolazepam. Induction time following MK in free-ranging Svalbard reindeer (*Rangifer tarandus platyrhynchus*) was reported to decrease from 14.3 to 6.5 minutes when the ketamine dose was increased from 1.08 to 2.26 mg kg^{-1}, although the medetomidine dose was doubled in the lower dose group (Arnemo & Aanes 2009). Induction time was also shorter in Persian fallow deer following thiafentanil combinations or etorphine–acepromazine, 2–3 or 5 minutes, respectively (Lapid et al. 2017). Shorter induction times are preferred during wildlife immobilizations to reduce stress, hyperthermia, injury or capture myopathy. Higher doses of both combinations may provide shorter onset, but effects on cardiopulmonary variables may be more pronounced.

Immobilization quality was excellent with both drug combinations, and this finding is in contrast to the muscle tremors and rigidity associated with potent opioids (Lapid et al. 2017).

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Other studies using the MK combination in deer species reported good immobilization quality (Arnemo et al. 2011; Bouts et al. 2011). Although immobilization quality was similar in MM and MK, the contribution of midazolam is unknown, as medetomidine alone (control group) was not evaluated.

The mean HR of deer in the present study was lower than in Persian fallow deer immobilized with etorphine- or thiafentanil-based combinations (47−50 *versus* 57−67 beats minute^{-1}) (Lapid et al. 2017). Lower HR can be attributed to the effects of medetomidine, which produces initial vasoconstriction resulting in hypertension and reflex bradycardia (Rankin 2015). Hyperthermia (RT $\geq$ 40.5 °C) was not observed in the present study. This finding is in contrast to a study in which three of 20 Persian fallow deer immobilized with thiafentanil−azaperone became hyperthermic (41.1−42.2 °C) (Lapid et al. 2017). Hyperthermia in the latter study was probably the result of increased muscle rigidity and tremors observed in that study.

α_2-Agonists in small ruminants can produce diffusion impairments and pulmonary edema (Rankin 2015), and may result in a decrease in SpO_2 in cervids via a similar mechanism. In the present study, significantly better SpO_2 values were obtained in MM (87%) *versus* MK (80%), and these values are higher than reported in Persian fallow deer administered opioid-based combinations (SpO_2 67−77%) (Lapid et al. 2017). This suggests that medetomidine-based combinations are less respiratory depressants than opioid-based combinations. Based on the SpO_2 values, the MM combination may be less respiratory depressant than the MK combination, however, the differences in SpO_2 could also be attributed to a lighter plane of immobilization produced by the MM combination. Similar mean SpO_2 values (88%) were reported in Svalbard reindeer following MK immobilization (Arnemo & Aanes 2009). In fallow deer immobilized in their natural habitat, with an average environmental temperature of 12 °C, with xylazine−tiletamine−zolazepam, SpO_2 values were 90−95% (Costa et al. 2017). The balance between better immobilization quality *versus* greater cardiopulmonary depression is challenging. Therefore, it was recommended to supply oxygen during immobilization of cervids (Evans et al. 2013).

Recovery times in the MK and MM groups were longer than in Chinese water deer (2.4 minutes) and in Norwegian reindeer (3.7 minutes) immobilized with MK (Arnemo et al. 2011; Bouts et al. 2011). The quicker recoveries observed in these studies are likely attributed to the route of atipamezole administration. In the Chinese water deer, atipamezole was administered intravenously (IV), and in the Norwegian reindeer half the dose was administered IV and the remainder IM. Recovery times from the medetomidine-based combinations in the present study were also longer than reported in Persian fallow deer immobilized with opioid-based protocols and administered naltrexone or diprenorphine (0.5−2.3 minutes) (Lapid et al. 2017).

The MM protocol has the advantage in that the effects of both drugs are completely reversible (Rankin 2015). However, a study in white-tailed deer reported no effect following IM administration of flumazenil (dissolved in dimethyl sulfoxide) on tiletamine−zolazepam reversal (Miller et al. 2004). Factors such as the solvent, insufficient dose or IM administration (instead of intravascular) could result in decreased flumazenil efficacy. In the present study, it was decided not to administer flumazenil as it was presumed that the effects of midazolam had worn off by the time the deer were due to be released. From a clinical point of view, recovery within 12−15 minutes is acceptable, so long as the animals are in a safe location. If quick recoveries are required in field immobilizations or in cases of emergency, then administration of flumazenil may be beneficial, although further studies to confirm this are required.

Limitations to this study include the small sample size, lack of a control treatment such as using medetomidine alone to investigate the efficacy of midazolam addition, lack of flumazenil administration to investigate the complete reversal of MM and the use of noninvasive techniques to measure oxygenation and blood pressure. Pulse oximetry can be affected by many factors and blood-gas analysis is a more accurate method of measuring oxygenation (Muller et al. 2012b).

Conclusion

Administration of MK and MM combinations to captive Persian fallow deer resulted in excellent immobilization quality, however, with onset times longer than reported with tiletamine−zolazepam or potent opioid combinations. SpO_2 values were low during immobilization with both combinations; therefore, oxygen supplementation should be available. Further studies of these combinations can be recommended to refine the doses and identify the physiologic effects in more detail.

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Authors' contributions

NA-M: conception, study design, data acquisition. BZ: data acquisition, data interpretation. RK: data acquisition. TB-A: study design, data analysis. YS-B: conception, study design, data interpretation, manuscript preparation. All authors revised the manuscript and approved the final version.

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Conflict of interest statement

Authors declare no conflict of interest.

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Appendix A. Scoring guidelines for induction, immobilization and recovery qualities

Score	Induction	Immobilization	Recovery
1 Poor	Did not become immobilized, second injection required	High muscle and jaw tone, significant spontaneous movements, not safe to take measurements	Slow recovery, thrashing, significant difficulty to stand
2 Fair	Initial excitation phase, time to immobilization > 15 minutes	High muscle and jaw tone, spontaneous movements	Slow recovery, very ataxic
3 Good	Calm but slow induction (longer than 5 minutes)	Moderate muscle tone, some spontaneous movements	Slow recovery, with some ataxia
4 Very good	Initial excitement, but quick induction (less than 5 minutes)	Muscle relaxation, no spontaneous movement, presence of ear reflex	Quick recovery, standing with some ataxia
5 Excellent	Calm and quick induction	Muscle relaxation, no spontaneous movement, no ear reflex	Quick recovery, standing with no ataxia

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